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Supporting Information - I

Novel aminoquinoline derivatives significantly reduce parasite load in *Leishmania infantum* infected mice

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Biological assays

***In vitro* antileishmanial activity – assay on promastigotes.** *Promastigote stage of L. infantum* strain MHOM/TN/80/IPT1 and *L. tropica* (MHOM/IT/2012/ISS3130) were cultured in Schneider's Drosophila medium (Lonza) supplemented with 10% heat-inactivated fetal calf serum (HyClone) at 22 °C. The complete medium used for antileishmanial activity assay was RPMI (EuroClone) supplemented with 10% heat-inactivated fetal calf serum (EuroClone), 20 mM Hepes, and 2 mM L-glutamine. To estimate the 50 % inhibitory concentration (IC_{50}), the MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) method was used with modifications.[1] Compounds were dissolved in DMSO and then diluted with medium to achieve the required concentrations. Drugs were placed in 96 wells round-bottom microplates and seven serial dilutions made. Amphotericin B was used as the reference anti-*Leishmania* drug. Parasites were diluted in complete medium to 5×10^6 parasites/mL and 100 µL of the suspension was seeded into the plates, incubated at 22 °C for 72 h and then 20 µL of MTT solution (5 mg/mL) was added into each well for 3 h. The plates were then centrifuged, the supernatants discarded and the resulting pellets dissolved in 100 µL of lysing buffer consisting of 20% (w/v) of a solution of SDS (Sigma), 40% of *N*,*N*-dimethylformamide (Merck) in H_2O. The absorbance was measured spectrophotometrically at a test wavelength of 550 nm and a reference wavelength of 650 nm. The results are expressed as IC_{50} which is the dose of compound necessary to inhibit parasite growth by 50%; each IC_{50} value is the mean ± standard deviation of separate experiments performed in duplicate.

***In vitro* intracellular amastigote susceptibility assays.** THP-1 cells (human acute monocytic leukemia cell line) were maintained in RPMI supplemented with 10% FBS (EuroClone), 50 µM 2-mercaptoethanol, 20 mM Hepes, 2 mM glutamine, at 37 °C in 5% CO_2. For *Leishmania* infections, THP-1 cells were plated at 5×10^5 cells/mL in 16-chamber Lab-Tek culture slides (Nunc) and treated with 0.1 µM phorbol myristate acetate (PMA, Sigma) for 48 h to achieve differentiation into macrophages. Cells were washed and infected with metacyclic *L. infantum* promastigotes at a macrophage/promastigote ratio of 1/10 for 24 h. Cell monolayers were then washed and incubated in the presence of test compounds for 72 h. Slides were fixed with methanol and stained with Giemsa. The results are expressed as the percentage of infected

macrophages in treated and non-treated cells determined by light microscopyand as IC_{50} which is the dose of compound necessary to inhibit parasite growth by 50%; each IC_{50} value is the mean ± standard deviation of separate experiments performed in duplicate.

Cytotoxicity against differentiated THP-1 cells. THP-1 cells were plated at 5×10^5 cells/mL in 96 wells flat bottom microplates and treated with 0.1 μM PMA for 48 h to achieve differentiation into macrophages. Cells were then treated for 72 hours with serial dilutions of test compounds and cell viability evaluated using the MTT assay already described.[2] The results are expressed as IC_{50}, which is the dose of compound necessary to inhibit cell growth by 50%.

Nitric oxide and ROS production. Immortalized mouse C57Bl/6 bone marrow derived macrophages (BMDM) were generated as described[3] and maintained in Dulbecco's minimal essential medium, DMEM (Euroclone, Italy) supplemented with 10% FBS (EuroClone), 2 mM L-glutamine, 20 mM HEPES at 37 °C in 5% CO_2. For NO and ROS production, BMDM were seeded (96-well plates; 1×10^5 cells/well) and incubated overnight. Cells were then primed with 50 U/ml of Interferon-gamma (IFN-γ) for 2h, and treated for 24 hours with different concentrations of **15** (5, 2.5, 1.25 μM) or **10** (2.5, 1.25, 0.625 μM). LPS (100 ng/mL) was used as positive control. Cell viability was determined by MTT assay. Nitric oxide production was measured in cell supernatants by Griess reaction.[4] The Griess reagents consisted in a mixture of equal parts of Reagent A (1% [w/v] sulphanilamide), and Reagent B (0.1% [w/v] naphthylethylenediamine dihydrochloride, and 2.5% [w/v] phosphoric acid). Fifty microliters of supernatants were mixed with an equal volume of Griess mixture and the nitrite levels were quantified by extrapolation from $NaNO_2$ standard curve. Absorbance was measured at 540 nm using a microplate reader (Synergy 4 microplate reader, Biotek, GE). ROS production was measured using the H_2DCFDA dye. After treatment of BMDM (as described above), the medium was discarded, the macrophages were washed with PBS, and incubated with H_2DCFDA (20μM in PBS) for 30 min in the dark at 37 °C in 5% CO_2. The supernatants were transferred into a flat-bottom black plate and fluorescence was measured spectrofluorometrically using an excitation wavelength of 485 nm and an emission wavelength of 528 nm by a Synergy 4, Biotek®. Statistical analyses were performed with GraphPad Prism 5 software by using 1-way ANOVA test followed by Bonferroni's post hoc test.

Tolerability studies in mice. Groups of four or five healthy female C57Bl/6 mice were treated per os (p.o.) or subcutaneous (s.c.) in a single dose with aminoquinolines suspended in 0.5% hydroxyethylcellulose-0.1% Tween 80 previously dissolved in DMSO (for p.o.) or dissolved in sunflower oil (for s.c.). Individual mouse behavior and appearance was monitored two times a day for 30 days. Compounds proved to be tolerable in mice if all mice survived 30 days after administration and showed normal appearance and behavior. The study followed the International Guiding Principles for biomedical research involving animals, and was reviewed by a local Ethics Committee and approved by the Veterinary Directorate at the Ministry of Agriculture and Environmental Protection of Serbia (decision no. 323-07-02444/2014-05/1).

Antileishmanial activity *in vivo*. A standard protocol using a short-term infection of Balb/c mice with *Leishmania infantum* was employed.[5] Briefly, a semi-purified suspension of 2×10^6 *Leishmania infantum* amastigotes (WHO reference strain: MHOM/TN/1980/IPT-1), was inoculated *via* the tail vein in groups of Balb/c mice weighing 18-20 g. On day 7 after infection the increase in parasite load was monitored by killing one animal from the control group. Liver was weighed, from which imprints were made and parasites counted against 500 liver cell nuclei. Their numbers were expressed as arbitrary units, i.e. the number of parasites per liver cell nucleus multiplied by the weight of the organ in mg. The compounds were dissolved and administered per os (**15** in 0.1%Tween/0.5%HEC in water; **10** in water) or s.c. (**15** in sunflower oil; **10** in water), for 4 or 5 consecutive days from day 9 after infection. A group of mice was left untreated and served as control. On days 13 or 14, the parasite load of killed mice was assessed as described above, and the mean parasite count of each treated group was expressed as a percentage of the mean parasite count of the control group. The study followed the International Guiding Principles for biomedical research involving animals (European Directive 2010/63/UE), and it was reviewed by a local Ethics Committee. The study was approved by the Directorate of Animal Health and Veterinary Drugs at the Ministry of Health of Italy (authorization no. 120/2015-PR).

Chemistry. Melting points were determined on a Boetius PMHK apparatus and were not corrected. IR spectra were recorded on a Thermo-Scientific Nicolet 6700 FT-IR diamond crystal spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini-200 spectrometer (at 200 and 50 MHz, respectively), and a Bruker Ultrashield Advance III spectrometer (at 500 and 125 MHz, respectively) in the indicated solvent (vide infra) using TMS as the internal standard. Chemical shifts are expressed in ppm (δ) values and coupling constants (J) in Hz. ESI–MS (HRMS) spectra of the synthesized compounds were acquired on a Agilent Technologies 1200 Series instrument equipped with Zorbax Eclipse Plus C18 (100 × 2.1 mm i.d. 1.8 μm) column and DAD detector (190-450 nm) in combination with a 6210 Time-of-Flight LC/MS instrument in positive and negative ion mode. The samples were dissolved in MeOH (HPLC grade). The selected values were as follows: capillary voltage 4 kV; gas temperature 350 °C; drying gas 12 L min^{-1}; nebulizer pressure 45 psig; fragmentator voltage: 70 V. Mass spectral analyses were done using electrospray ionization in positive ion mode on a Surveyor separations module coupled to a ThermoFinnigan TSQ AM triple quadrupole mass spectrometer. Gas chromatography tandem mass spectrometry (GC-MS) analyses were performed on an Agilent 7890A GC (Agilent) system equipped with a 5975C inert XL EI/CI MSD and a flame ionization detector (FID) connected by capillary flow technology through a 2-way splitter with make-up gas. An HP-5 MS capillary column (Agilent Technologies, 25 mm i.d., 30 m length, 0.25 μm film thickness) was used. The flash chromatography was performed on Biotage SP1 system equipped with UV detector and FLASH 12+, FLASH 25+ or FLASH 40+ columns charged with KP-SIL (40 – 63 μm, pore diameter 60 Å), KP-C18-HS (40 – 63 μm, pore diameter 90 Å) or KP-NH (40 – 63 μm, pore diameter 100 Å) as an adsorbent. Elemental analyses were realized with an Elemental Vario EL III microanalyser. All tested compounds were fully characterized and their purity was >95% (as determined by HPLC).

Methods for HPLC purity analyses

Compounds were analyzed for purity (HPLC) using a Agilent 1200 HPLC system equipped with Quat Pump (G1311B), Injector (G1329B) 1260 ALS, TCC 1260 (G1316A) and Detector 1260 DAD VL+ (G1315C). HPLC analysis was performed in two diverse systems for each compound. **Method A:** Zorbax Eclipse Plus C18 2.1 x 100 mm, 1.8μ, S.N. USUXU04444 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A)

and methanol (B). The analysis were performed at the UV max of the compounds (at 254 nm for compounds **4**, **6** and **21**, 270 nm for compounds **3** and **5**, 290 nm for **22** and **23** and 330 nm for compounds **1**, **2**, **10, 24** and **25**) to maximize selectivity. Compounds were dissolved in methanol, final concentrations were ~1 mg/mL. Flow rate was 0.2 mL/min.

Compounds **1-6** and **21** were eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-14 min 5%A→ 95%A, 14-20 min 95%A.

Compound **10** was eluted using gradient protocol: 0-1.5 min 95%A, 1.5-5 min 95%A→ 5%A, 5-16 min 5%A, 16-18 min 5%A→ 95%A, 18-20 min 95%A.

Compound **22** was eluted using gradient protocol: 0-1 min 95%A, 1-3 min 95%A→ 5%A, 3-7 min 5%A, 7-8 min 5%A→ 95%A, 8-9 min 95%A.

Compound **23** was eluted using gradient protocol: 0-2 min 95%A, 2-4 min 95%A→ 5%A, 4-10 min 5%A, 10-11 min 5%A→ 95%A, 11-12 min 95%A.

Compounds **24** and **25** were eluted using gradient protocol: 0-1 min 95%A, 1-2 min 95%A→ 5%A, 2-10 min 5%A, 10-11 min 5%A→ 95%A, 11-12 min 95%A.

Method B: Zorbax Eclipse Plus C18 2.1 x 100 mm, 1.8µ, S.N. USUXU04444 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and acetonitrile (B). The analysis were performed at the UV max of the compounds (at 254 nm for compound **21**, 270 nm for compounds **3**, **4** and **6** and 330 nm for compounds **1**, **2**, **5**, **10**, **24** and **25**) to maximize selectivity. Compounds were dissolved in methanol, final concentrations were ~1 mg/mL. Flow rate was 0.2 mL/min.

Compounds **1-6** and **21** were eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-14 min 5%A→ 95%A, 14-20 min 95%A.

Compound **10** was eluted using gradient protocol: 0-1.5 min 95%A, 1.5-5 min 95%A→ 5%A, 5-16 min 5%A, 16-18 min 5%A→ 95%A, 18-20 min 95%A.

Compound **24** was eluted using gradient protocol: 0-1 min 95%A, 1-3 min 95%A→ 5%A, 3-8 min 5%A, 8-10 min 5%A→ 95%A, 10-11 min 95%A.

Compound **25** was eluted using gradient protocol: 0-1 min 95%A, 1-3 min 95%A→ 5%A, 3-8 min 5%A, 8-10 min 5%A→ 95%A.

Method C: Zorbax Eclipse Plus C18 4.6 x 150mm, 1.8µ, S.N. USWKY01594 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and methanol (B). The analysis were performed at the UV max of the compounds (at 330 nm for

compound **15**) to maximize selectivity. Compounds were dissolved in methanol, final concentrations were ~1 mg/mL. Flow rate was 0.5 mL/min.

Compound **15** was eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-14 min 5%A→ 95%A, 14-16 min 95%A.

Method D: Poroshell 120 EC-C18, 4.6 x 50mm, 2.7µ, S.N. USCFU07797 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and acetonitrile (B). The analysis were performed at the UV max of the compounds (at 254 nm for compound **15**) to maximize selectivity. Compounds were dissolved in methanol, final concentrations were ~1 mg/mL. Flow rate was 0.5 mL/min.

Compound **15** was eluted using gradient protocol: 0-1 min 95%A, 1-6 min 95%A→ 5%A, 6-11 min 5%A, 11-13 min 5%A→ 95%A, 13-17 min 95%A.

Method E: Poroshell 120 EC-C18, 4.6 x 50mm, 2.7µ, S.N. USCFU07797 was used as the stationary phase. Eluent was made from the following solvents: 0.2% formic acid in water (A) and methanol (B). The analysis was performed at the UV max of the compounds (290 nm for compounds **22** and **23**) to maximize selectivity. Compound was dissolved in methanol, final concentration was ~1 mg/mL. Flow rate was 0.5 mL/min.

Compounds **22** and **23** were eluted using gradient protocol: 0-1 min 95%A, 1-1.5 min 95%A→ 5%A, 1.5-6min 5%A, 6-7 min 5%A→ 95%A, 7-8 min 95%A.

Synthetic procedures

Procedure A: General procedure for nucleophilic substitution.[6]

A solution of **31**[7] (1 equiv) in DCM was cooled to 0 ºC, followed by addition of amine (1.5 equiv) and Et_3N (1.5 equiv). The reaction mixture was stirred on ice bath for 15 minutes, warmed to r.t. and after another 15 minutes heated to reflux for 1h. The mixture was transferred to a separation funnel, water was added and desired product extracted with DCM. Combined organic layers were dried over anh. $MgSO_4$ and the solvent was removed under reduced pressure.

Procedure B: General procedure for reduction using tin(II)-chloride.

Using slightly modified procedure from literature[7], a mixture of 3-nitroquinoline derivative (1 equiv) and $SnCl_2$ (5 equiv) in EtOH was stirred at r.t. under Ar atmosphere for 2 h. Solvent was removed under reduced pressure, followed by addition of sat. $NaHCO_3$. Crude product was extracted several times with EtOAc. Combined extracts were washed with brine, dried over anh. $MgSO_4$ and the solvent was evaporated under reduced pressure.

Procedure C: General procedure for Boc-protecting group removal with TFA.

A solution of amine in TFA/DCM mixture (v:v; 1:10) was stirred at r.t. overnight. Solvents were evaporated under reduced pressure and the residue was dissolved in DCM. The organic layer was washed several times with 2.5M NaOH and finally with water, dried over anh. $MgSO_4$ and the solvent was removed under reduced pressure.

Procedure D: General procedure for reductive amination.

Amine (1.2-1.5 equiv) and appropriate aldehyde (1 equiv) were dissolved in MeOH/DCM mixture (v:v; 2:1), glac. AcOH (1.5 equiv) was added, and the mixture was stirred under Ar atmosphere at r.t. After 3 h, $NaBH_4$ (6 equiv) was added, and stirring was continued for another 18 h. Solvent was removed under reduced pressure, and the residue was dissolved in DCM. The organic layer was washed with 2M aqueous NH_3 and extracted with DCM. The combined organic layers were washed with brine and dried over anh. Na_2SO_4. Finally, the solvent was evaporeted under reduced pressure.

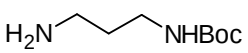
Procedure E: General procedure for Buchwald-Hartwig amination[8]

A suspension of $Pd(OAc)_2$ (4.00 mol %) and SPhos (8.00 mol %) in dioxane was purged with Ar and stirred at r.t. After three minutes, solution of **45** (1 equiv) in dioxane, an appropriate amine (1.5 equiv) and K_3PO_4 (2.5 equiv) were added. The mixture was heated at 85 °C for 24 h in a

sealed tube. After filtration the crude product was purified using column chromatography (dry flash, SiO_2, eluent EtOAc/MeOH and flash, Biotage SP1, NH column, elunet EtOAc/MeOH).

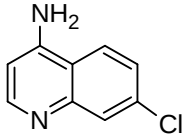
N-(7-chloroquinolin-4-yl)propane-1,3-diamine (**AQ3**) and *N*-(quinolin-4-yl)butane-1,4-diamine (**AQ8**) were prepared according to known procedures.

tert-Butyl (3-aminopropyl)carbamate (S1).



According to the procedure described in literature[9], a solution of Boc_2O (518.2 mg, 2.374 mmol) in DCM (10 mL) was added dropwise to a solution of propane-1,3-diamine (1 mL, 12 mmol) in DCM (40 mL). Reaction mixture was stirred at r.t. for 24h. Thereafter the solvent was removed under reduced pressure and the product was purified using column chromatography (dry-flash, SiO_2, eluent DCM/MeOH gradient 6/4 → MeOH). Final product **S1** was obtained as a yellowish oil (228.0 mg, 55%). IR (ATR): 3350m, 2976s, 2934m, 1692s, 1525s, 1391m, 1366m, 1277m, 1252m, 1173s, 1060w, 871w, 780w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 4.95 (bs, H-N), 3.24-3.20 (m, 2H, $NH_2CH_2CH_2CH_2$-), 2.79 (t, 2H, J = 6.7, NH_2CH_2-), 1.98 (bs, -NH_2), 1.66-1.61 (m, 2H, $NH_2CH_2CH_2$-), 1.44 (s, 9H, -$NHCOOC(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 156.19, 79.11, 39.47, 38.30, 33.01, 28.39. HRMS: *m/z* 175.14407 corresponds to molecular formula $C_8H_{18}N_4O_2H^+$ (error in ppm -0.20).

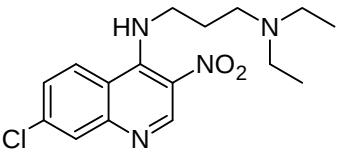
7-Chloroquinolin-4-amine (S2).[10]



To the solution of 4,7-dichloroquinoline (676 mg, 3.41 mmol) in phenol (3.2 g, 34 mmol) stirring in two-necked flask at 110 °C, ammonium-carbonate (1.64 g, 17.1 mmol) was added in portions in a manner determined by intensity of foam developing in the flask. When addition was completed, the mixture was stirred at 165 °C for 3h. After cooling to r.t. diethylether was added. The solution was washed with 10% aqueous NaOH, extracted with diethylether and dried over anh. Na_2SO_4. The product was purified using column chromatography (dry-flash, SiO_2, eluent DCM /MeOH). Final product **S2** was obtained as white solid (602 mg, 99%). M.p. = 137 – 139 ºC. IR (KBr): 3459s, 3358s, 3241s, 2460m, 1698m, 1639s, 1612s, 1576s, 1508s, 1445s, 1378m, 1327m, 1284m, 1201m, 1130m, 1078m, 910m, 879m, 855m, 839m, 813m, 761m, 675w, 644w cm^{-1}. ^1H NMR (500 MHz, CD_3OD, δ): 8.26 (d, J = 5.5, H-C(2)), 8.05 (d, J = 8.9, H-C(5), 7.77 (d, J = 2.1, H-C(8)), 7.37 (dd, J_1 = 9.0, J_2 = 2.2, H-

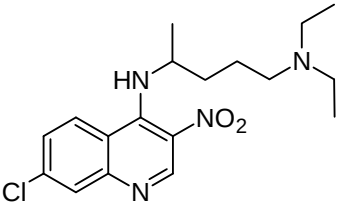
C(6)), 6.62 (d, J = 5.3, H-C(3)). ^{13}C NMR (125 MHz, CD_3OD, δ): 155.55, 152.11, 150.18, 136.66, 127.55, 125.93, 125.14, 118.48, 104.03. HRMS: *m/z* 179.03700 corresponds to molecular formula $C_9H_7ClN_2H^+$ (error in ppm -0.32).

_N_'-(7-Chloro-3-nitroquinolin-4-yl)-_N_,_N_-diethylpropane-1,3-diamine (1).



Compound **1** was synthesized from **31** (50.0 mg, 0.206 mmol) and 3-diethylamino-1-propilamine (0.05 mL, 0.32 mmol) by procedure A. The product was purified using column chromatography (dry-flash, SiO_2, eluent MeOH, EtOAc/(MeOH/NH_3=9/1) gradient 9/1 → 1/1 and flash chromatography, Biotage SP1, NH column, eluent EtOAc/Hex gradient 8/2). Final product **1** was obtained as a bright yellow solid (53.8 mg, 78%); softens at 50 ºC. IR (ATR): 3122m, 2968s, 2876m, 2839m, 1566s, 1517s, 1448m, 1396m, 1342m, 1284m, 1254s, 1215m, 1191m, 1157m, 1116m, 1088w, 1021w, 980w, 958w, 924w, 892w, 819m, 774w, 719w, 596w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 9.97 (s, H-N), 9.26 (s, H-C(2)), 8.19 (d, J = 8.9, H-C(5)), 7.95 (d, J = 2.3, H-C(8)), 7.40 (dd, J_1 = 9.0, J_2 = 2.2, H-C(6)), 3.85 (q, 2H, J = 6.0, ArNHCH_2-), 2.66 (t, 2H, J = 6.2, -CH_2N(CH_2CH_3)$_2$), 2.59 (q, 4H, J = 7.1, -N(C$H_2$$CH_3$)$_2$), 1.94-1.89 (m, 2H, ArNHCH$_2$CH_2-), 1.04 (t, 6H, J = 7.1, -N(CH_2CH_3)$_2$). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 150.88, 149.73, 148.64, 138.32, 129.31, 127.38, 126.12, 125.82, 118.07, 50.72, 48.57, 46.98, 27.60, 11.31. HRMS: *m/z* 337.14259 corresponds to molecular formula $C_{16}H_{21}ClN_4O_2H^+$ (error in ppm 0.03); *m/z* 169.07533 corresponds to molecular formula $C_{16}H_{21}ClN_4O_2H_2^{2+}$ (error in ppm 2.39). HPLC purity (λ = 330 nm) method A: RT 9.953 min, area 98.91%; method B: RT 8.598 min, area 95.44%.

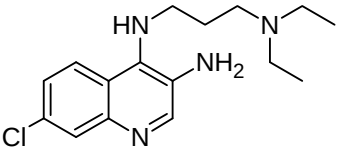
_N_^{4}-(7-Chloro-3-nitroquinolin-4-yl)-_N_^{1},_N_^{1}-diethylpentane-1,4-diamine (2).



Compound **2** was synthesized from **31** (75 mg, 0.31 mmol) and 2-amino-5-diethylaminopentane (0.09 mL, 0.46 mmol) by procedure A. The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/(MeOH/NH_3=9/1) gradient 8/2 → 1/1 and flash chromatography, Biotage SP1, NH column, eluent EtOAc/MeOH gradient EtOAc → 97/3). Final product **2** was obtained as a bright yellow oil (88.0 mg, 78%). IR (ATR): 3272w, 2968m, 2930m, 2870w, 2804w, 1606m, 1578s, 1530m, 1450m, 1410m, 1382m, 1276m, 1249m, 1228m,

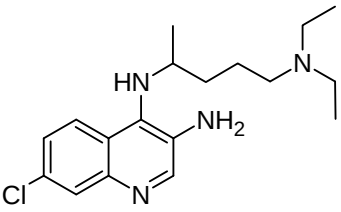
1189w, 1155m, 1110w, 950w, 883w, 822w, 778w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 9.46 (d, *J* = 8.7, H-N), 9.35 (s, H-C(2)), 8.13 (d, *J* = 9.2, H-C(5)), 7.97 (d, *J* = 2.0, H-C(8)), 7.43 (dd, J_1 = 9.2, J_2 = 2.3, H-C(6)), 4.4.-4.32 (m, 1H, ArNHC*H*(CH_3)-), 2.46 (q, 4H, *J* = 7.1, -N(C$H_2$$CH_3$)$_2$), 2.38 (t, 2H, *J* = 7.3, -CH_2N(CH_2CH_3)$_2$), 1.82-1.69 (m, 2H, ArNHCH(CH_3)CH_2-), 1.58-1.46 (m, 5H, -C$H_2$$CH_2$N($CH_2CH_3$)$_2$, ArNHCH(C$H_3$)-), 0.96 (t, 6H, *J* = 7.2, -N(CH_2CH_3)$_2$). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 151.27, 150.38, 148.56, 138.71, 129.56, 127.75, 126.52, 126.19, 117.79, 54.63, 52.24, 46.74, 36.77, 23.73, 22.12, 11.51. HRMS: *m/z* 365.17392 corresponds to molecular formula $C_{18}H_{25}ClN_4O_2H^+$ (error in ppm 0.10); *m/z* 183.09120 corresponds to molecular formula $C_{18}H_{25}ClN_4O_2H_2^{2+}$ (error in ppm 3.42). HPLC purity (λ = 330 nm) method A: RT 10.947 min, area 98.75%; method B: RT 8.985 min, area 97.28%.

7-Chloro-N^4-[3-(diethylamino)propyl]quinoline-3,4-diamine (3).



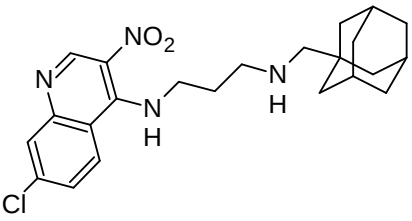
Compound **3** was prepared by procedure B using **1** (10.3 mg, 0.0306 mmol) and $SnCl_2$ (29.0 mg, 0.153 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent DCM/(MeOH/NH_3=9/1) = 9/1). Final product **3** was obtained as a brown oil (3.8 mg, 40%). IR (ATR): 3313s, 2969s, 2930s, 2817m, 1596s, 1564s, 1468m, 1380s, 1344s, 1198m, 1166w, 1133m, 1075m, 988w, 897w, 815m, 767w, 673w, 548w, 436w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.41 (s, H-C(2)), 7.92 (d, *J* = 2.1, H-C(8)), 7.85 (d, *J* = 9.2, H-C(5)), 7.35 (dd, J_1 = 9.2, J_2 = 2.1, H-C(6)), 4.77 (bs, H-N), 4.08 (bs, -NH_2), 3.38 (t, 2H, *J* = 6.0, ArNHCH_2), 2.73-2.68 (m, 6H, -CH_2N(CH_2CH_3)$_2$, -N(C$H_2$$CH_3$)$_2$), 1.90-1.85 (m, 2H, ArNHCH_2CH_2-), 1.12 (t, 6H, *J* = 7.2, -N(CH_2CH_3)$_2$). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 144.58, 144.24, 135.92, 131.03, 130.74, 128.58, 126.21, 122.17, 121.93, 51.14, 46.38, 45.27, 26.88, 10.66. HRMS: *m/z* 307.16817 corresponds to molecular formula $C_{16}H_{23}ClN_4H^+$ (error in ppm -0.76); *m/z* 154.08791 corresponds to molecular formula $C_{16}H_{23}ClN_4H_2^{2+}$ (error in ppm 0.48). HPLC purity (λ = 270 nm) method A: RT 9.241 min, area 97.15%; method B: RT 7.692 min, area 95.76%.

7-Chloro-N^4-[4-(diethylamino)-1-methylbutyl]quinoline-3,4-diamine (4).



Compound **4** was prepared by procedure B using **2** (64.7 mg, 0.177 mmol) and $SnCl_2$ (168.1 mg, 0.8865 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent DCM/(MeOH/NH_3=9/1) = 9/1). Final product **4** was obtained as a brown oil (35.8 mg, 60%). IR (ATR): 3323s, 2968s, 2816m, 1597s, 1564s, 1488m, 1378s, 1347s, 1196w, 1131m, 984w, 900w, 876w, 820m, 767m, 548w, 429w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.45 (s, H-C(2)), 7.94 (d, J = 2.3, H-C(8)), 7.73 (d, J = 8.9, H-C(5)), 7.37 (dd, J_1 = 8.9, J_2 = 2.3, H-C(6)), 3.78 (bs, -NH_2 exchangeable with D_2O), 3.56 (bs, H-N exchangeable with D_2O), 2.57-2.37 (m, 7H, ArNHCH(CH_3)-, -CH_2N(CH_2CH_3)$_2$, -N(C$H_2$$CH_3$)$_2$), 1.68-1.49 (m, 4H, ArNHCH(CH_3)CH_2-, ArNHCH(CH_3)CH_2CH_2-), 1.14 (d, 3H, J = 6.2, ArNHCH(CH_3)-), 1.00 (t, 6H, J = 7.1, -N(CH_2CH_3)$_2$). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 144.64, 144.42, 134.89, 131.52, 131.18, 128.75, 126.56, 122.89, 121.77, 52.90, 51.18, 46.87, 36.42, 23.97, 21.94, 11.47. HRMS: *m/z* 335.19970 corresponds to molecular formula $C_{18}H_{27}ClN_4H^+$ (error in ppm 0.00); *m/z* 168.10399 corresponds to molecular formula $C_{18}H_{27}ClN_4H_2^{2+}$ (error in ppm 2.97). HPLC purity method A (λ = 254 nm): RT 8.866 min, area 95.57%; method B (λ = 270 nm): RT 7.883 min, area 95.56%.

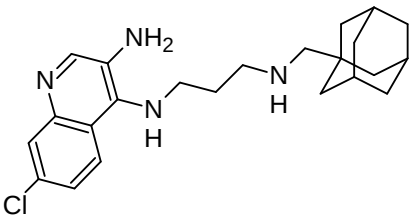
***N*-(1-adamantylmethyl)-*N*'-(7-chloro-3-nitroquinolin-4-yl)propane-1,3-diamine (5).**



A solution of **33** (62.0 mg, 0.279 mmol) in DCM (3 mL) was cooled to 0 ºC. Then, **31** (45.2 mg, 0.186 mmol) was added and stirring continued at same temperature for 15 min. Mixture was allowed to warm to r.t. and after another 15 minutes heated to reflux for 2h. Water was added and product extracted several times with DCM. Combined organic layers were dried over anh. $NaSO_4$ and the solvent was evaporated under reduced pressure. The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc → EtOAc/MeOH = 1/1 and flash chromatography, Biotage SP1, NH column, eluent EtOAc/Hex gradient 6/4 → 8/2). Final product **5** was obtained as a bright yellow oil (57.5 mg, 72%). IR (ATR): 3334w, 3246w, 2901s, 2844s, 1582s, 1530m, 1449m, 1416m, 1342m, 1279m, 1248m, 1218m, 1187m, 1155m, 1118m, 952w, 899w, 826w, 775w, 704w, 626w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 9.74 (bs, H-N

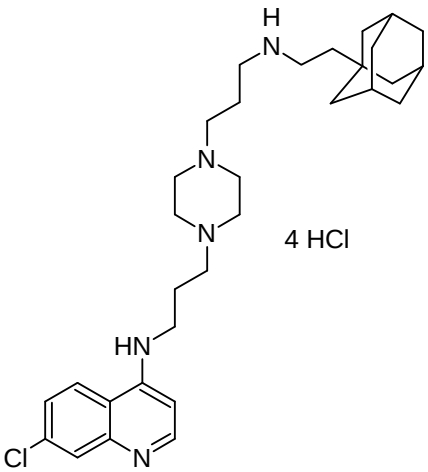
exchangeable with D_2O), 9.32 (s, H-C(2)), 8.26 (d, *J* = 9.2, H-C(5)), 7.96 (d, *J* = 2.1, H-C(8)), 7.41 (dd, J_1 = 9.0, J_2 = 2.2, H-C(6)), 3.98-3.95 (m, 2H, ArNHCH_2-), 2.80 (t, 2H, *J* = 6.3, -CH_2NHCH$_2$Ad), 2.24 (s, 2H, -CH_2Ad), 1.97-1.92 (m, 5H, ArNHCH$_2$CH_2-, -Ad), 1.72-1.70 (m, 3H, -Ad), 1.63-1.60 (m, 3H, -Ad), 1.48 (d, 6H, *J* = 2.1, -Ad). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 151.20, 150.38, 148.63, 138.59, 129.39, 127.96, 126.14, 125.90, 118.00, 62.96, 48.14, 47.89, 40.86, 37.16, 33.47, 30.73, 28.41. HRMS: *m/z* 429.20526 corresponds to molecular formula $C_{23}H_{29}ClN_4O_2H^+$ (error in ppm 0.20); *m/z* 215.10664 corresponds to molecular formula $C_{23}H_{29}ClN_4O_2H_2^{2+}$ (error in ppm 1.92). HPLC purity method A (λ = 270 nm): RT 11.811 min, area 95.51%; method B (λ = 330 nm): RT 10.885 min, area 97.86%.

N^4-{3-[(1-adamantylmethyl)amino]propyl}-7-chloroquinoline-3,4-diamine (6).



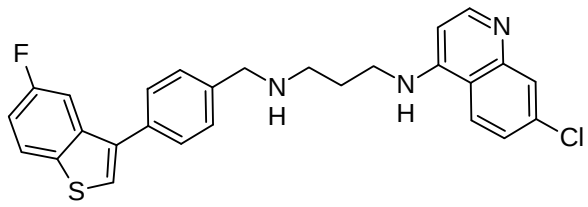
Compound **6** was synthesized by procedure B using **5** (36.7 mg, 0.086 mmol) and $SnCl_2$ (81.2 mg, 0.428 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent DCM/(MeOH/NH_3=9/1) = 9/1). Final product **6** was obtained as a yellowish foam (24.2 mg, 71%); softens at 30-32 ºC. IR (ATR): 3312m, 2901s, 2845s, 1597m, 1564m, 1453m, 1344m, 1198w, 1119w, 897w, 814w, 734w, 548w cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.43 (s, H-C(2)), 7.93 (d, *J* = 2.1, H-C(8)), 7.84 (d, *J* = 9.2, H-C(5)), 7.34 (dd, J_1 = 9.2, J_2 = 2.1, H-C(6)), 4.03 (bs, H-N exchangeable with D_2O), 3.33 (t, 2H, J = 6.1, ArNHCH_2-), 2.86 (t, 2H, J = 6.0, -CH_2NHCH$_2$Ad), 2.32, (s, 2H, -CH_2Ad), 1.98 (bs, 3H, -Ad), 1.86-1.81 (m, 2H, ArNHCH$_2$CH_2-), 1.74-1.72 (m, 3H, -Ad), 1.66-1.63 (m, 3H, -Ad), 1.56 (d, 6H, J = 2.4, -Ad). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 144.54, 144.30, 135.88, 131.32, 131.01, 128.63, 126.37, 122.34, 122.11, 63.53, 49.65, 46.01, 41.09, 37.15, 33.32, 29.84, 28.40. HRMS: *m/z* 399.22992 corresponds to molecular formula $C_{23}H_{31}ClN_4H^+$ (error in ppm - 2.71); *m/z* 200.11926 corresponds to molecular formula $C_{23}H_{31}ClN_4H_2^{2+}$ (error in ppm 0.62). HPLC purity method A (λ = 254 nm): RT 10.495 min, area 96.03%; method B (λ = 270 nm): RT 9.666 min, area 98.63%.

4-({3-[4-(3-{[2-(1-adamantyl)ethyl]ammonio}propyl)piperazinediium-1-yl]propyl}amino)-7-chloroquinolinium tetrachloride (10).



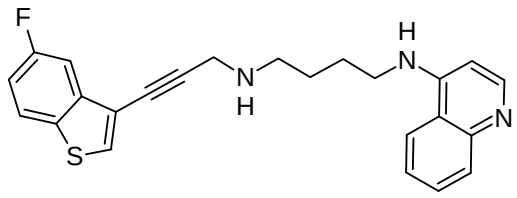
Amine **38** (50 mg, 0.098 mmol) was suspended in 0.5 mL EtOH, followed by addition of EtOH/HCl solution (2 mL, 25%) and the reaction mixture was vigorously stirred 24h at r.t. Formed solid was filtered and washed well with 96% EtOH (5 mL) and Et_2O (5 mL). Upon drying at r.t. under reduced pressure desired salt was obtained (55 mg, 85%). M.p. > 280 ^{o}C. IR (ATR): 3383s, 3107w, 2902s, 2846m, 2657w, 2516w, 2437w, 2367w, 2325w, 2191w, 2121w, 2029w, 2006w, 1988w, 1965w, 1922w, 1615s, 1451s, 1362m, 1246w, 1216m, 1170w, 1141w, 1097w, 1052w, 1022w, 954m, 905m, 815m, 766m, 656w, 602w cm^{-1}. ^{1}H NMR (500 MHz, D_2O): 8.36 (d, 1H, *J* = 7.0 Hz, H-C(2)), 8.20 (d, 1H, *J* = 9.3 Hz, H-C(5)), 7.90 (d, 1H, *J* = 1.6 Hz, H-C(8)), 7.69 (dd, 1H, *J* = 1.9 Hz, *J* = 9.0 Hz, H-C(6)), 6.87 (d, 1H, *J* = 7.0 Hz, H-C(3)), 3.80-3.70 (m, 2H, ArNHC*H*$_2$-), 3,70-3,55 (m, 8H, -NH$^+$(C*H*$_2$C*H*$_2$)$_2$NH$^+$-), 3,50-3,40 (m, 2H, ArNHCH$_2$CH$_2$C*H*$_2$NH$^+$(CH$_2$CH$_2$)$_2$NH$^+$-), 3,35-3,25 (m, 2H, -NH(CH$_2$CH$_2$)$_2$NH$^+$C*H*$_2$CH$_2$CH$_2$NH$_2^+$CH$_2$CH$_2$Ad), 3,20-3,05 (m, 4H, -C*H*$_2$NH$_2^+$CH$_2$CH$_2$Ad, -C*H*$_2$CH$_2$Ad), 2.35-2.25 (m, 2H, ArNHCH$_2$C*H*$_2$-), 2.20-2.10 (m, 2H, -C*H*$_2$CH$_2$NH$_2^+$CH$_2$CH$_2$Ad), 2.00-1.90 (m, 3H, -Ad), 1.80-1.60 (m, 6H, -Ad), 1.60-1.50 (m, 6H, -Ad), 1.50-1.40 (m, 2H, -C*H*$_2$Ad). ^{13}C NMR (125 MHz, D_2O): 156.11; 142.34; 139.40; 138.06; 127.56; 124.02; 119.16; 115.34; 98.32; 54.28; 53.53; 49.25; 49.06; 44.20; 43.56; 41.34; 40.02; 39.37; 36.26; 31.06; 28,14, 22.50, 21.01. HRMS: *m/z* 524.35077 corresponds to molecular formula $C_{31}H_{46}ClN_5H^+$ (error in ppm -1.30). HPLC purity (λ=330 nm): method A: RT 9.973, area 98.31%; method B: RT 8.296, area 95.32%. Anal. ($C_{31}H_{46}ClN_5 \times 4HCl \times 3.5H_2O$) Calcd: C, 50.79; H, 7.84; N, 9.55. Found: C, 50.89; H, 7.80; N, 9.62.

***N*-(7-chloroquinolin-4-yl)-*N*'-[4-(5-fluoro-1-benzothiophene-3-yl)benzyl]propane-1,3-diamine (15).**



Compound **15** was prepared by procedure D, using aldehyde **39**[11] (118 mg, 0.460 mmol), amine **AQ3** (162.8 mg, 0.6906 mmol), glac. AcOH (40 μL, 0.7 mmol), $NaBH_4$ (104.5 mg, 2.762 mmol) and MeOH/ DCM (18 mL, 2:1, v/v). The product was purified using column chromatography (flash, Biotage SP1, NH column, eluent hexane/EtOAc gradient 2/8 → EtOAc, EtOAc/MeOH gradient 95/5 → 1/1, MeOH; flash, Biotage SP1, SiO2 column, eluent DCM /MeOH+NH_3 (9/1) gradient 95/5 → 3/7). Final product **15** was obtained as a pale yellow foam (156.5 mg, 71%). M.p. = 39 – 40 ºC. IR (ATR): 3239w, 3062w, 2935w, 2844w, 1583s, 1537m, 1492w, 1437m, 1368w, 1332w, 1282w, 1251w, 1197w, 1138w, 1114w, 883w, 853w, 806m, 784w, 650w cm^{-1}. ^{1}H NMR (500MHz, $CDCl_3$): 8.50 (d, J = 5.3, H-C(2')), 7.92-7.90 (m, H-C(8')), 7.84 (dd, J_1 = 4.8, J_2 = 8.9, H-C(7)), 7.59-7.53 (m, 5H, 2H-Ar, H-C(4), H-C(5') and H-N exchangeable with D_2O), 7.50 (s, H-C(2)), 7.48-7.44 (m, 2H-Ar), 7.19-7.11 (m, 2H, H-C(6) and H-C(6')), 6.32 (d, J = 5.2, H-C(3')), 3.92 (s, 2H, ArCH_2NH-), 3.45-3.40 (m, 2H, ArNHCH_2-), 3.05-3.01 (m, 2H, $ArCH_2NHCH_2$-), 2.02-1.95 (m, 2H $ArCH_2NHCH_2CH_2$-), 1.86 (bs, H-N exchangeable with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$): 161.13 (d, J = 240.7), 152.13, 150.40, 149.15, 139.14, 138.98, 137.37 (d, J = 4.7), 136.03, 134.70, 134.58, 128.83, 128.74, 128.53, 125.86, 124.79, 124.05 (d, J = 8.5), 122.04, 117.50, 113.40 (d, J = 25.6), 108.45 (d, J = 23.7), 98.32, 54.01, 49.32, 43.97, 27.45. HRMS: *m/z* 476.13504 corresponds to molecular formula $C_{27}H_{23}ClN_3SFH^+$ (error in ppm -1.60), *m/z* 238.57136 corresponds to molecular formula $C_{27}H_{23}ClN_3SFH_2^{2+}$ (error in ppm -0.75). HPLC purity: method C (λ = 330 nm): RT 9.741, area 96.57%; method D (λ = 254 nm): RT 5.816, area 95.63%.

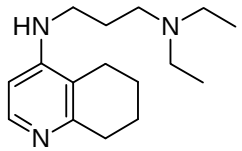
***N*-[3-(5-fluoro-1-benzothien-3-yl)prop-2-yn-1-yl]-*N*'-quinolin-4-ylbutane-1,4-diamine (21).**



Solution of **40** (11.7 mg, 0.0507 mmol) in DMF (0.1 mL), $PdCl_2(PPh_3)_2$ (2.1 mg, 6.0 mol%), PPh_3 (2.6 mg, 20 mol%), solution of **41** (10.7 mg, 0.0422 mmol) in DMF (0.1 mL), CuI (0.6 mg, 6 mol%) and

Et_2NH (78 μL, 0.71 mmol) were added to a dry microwave tube (0.2-0.5 mL) under Ar atmosphere. The mixture was heated in microwave reactor (*Biotage Initiator 2.5 apparatus*) at 120 °C for 25 minutes. After cooling to r.t. the reaction mixture was transferred to the separation funnel and DCM was added. Organic layer was washed with brine (with addition of 1 drop of aqueous NH_3) and dried over anh. Na_2SO_4. Crude product was purified using column chromatography (flash, Biotage SP, NH column, 12+M, eluent hexane/EtOAc gradient 2/8 → EtOAc, EtOAc/MeOH gradient 9/1 → 1/1). Final product **21** was obtained as yellow oil (5.4 mg, 27%). IR (ATR): 3440w, 3250m, 3067m, 2930m, 2858m, 1582s, 1542m, 1442m, 1396w, 1374w, 1340m, 1298w, 1248w, 1196w, 1129w, 1100w, 1036w, 947w, 874w, 808w, 764m, 736w, 650w cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, δ): 8.53 (d, *J* = 5.6, H-C(2')), 8.01-7.93 (m, H-C(8')), 7.83-7.71 (m, 2H, H-C(5') and H-C(7)), 7.70-7.50 (m, 3H, H-C(7'), H-C(4) and H-C(2)), 7.45-7.34 (m, H-C(6')), 7.21-7.08 (m, H-C(6)), 6.40 (d, *J* = 5.6, H-C(3')), 5.72 (bs, *H*-N), 3.78 (s, 2H, -C*H*$_2$C≡C-Ar), 3.41-3.29 (m, 2H, ArNHC*H*$_2$-), 2.98-2.87 (m, 2H, ArNH$(CH_2)_3$C*H*$_2$-), 2.01-1.68 (m, 5H, ArNHCH_2C*H*$_2$C*H*$_2$- and *H*-N). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 161.21 (d, *J* = 241.9), 150.66, 150.04, 147.99, 134.12, 131.93, 129.50, 129.05, 124.53, 123.82 (d, *J* = 9.0), 119.62, 118.74, 117.95, 113.99 (d, *J* = 25.3), 111.78, 108.52 (d, *J* = 23.5), 98.55, 90.30, 76.47, 48.12, 43.18, 39.11, 27.57, 26.43. HRMS: *m/z* 404.15750 corresponds to molecular formula $C_{24}H_{22}FN_3SH^+$ (error in ppm -4.00). HPLC purity (λ = 254 nm): method A: RT 10.106, area 96.11%; method B: RT 8.432, area 95.69%.

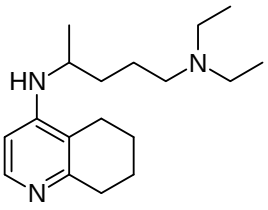
N^1,N^1-diethyl-N^3-(5,6,7,8-tetrahydroquinolin-4-yl)propane-1,3-diamine (22).



Compound **22** was prepared by procedure E, using $Pd(OAc)_2$ (1.4 mg, 0.0064 mmol), SPhos (5.2 mg, 0.013 mmol), **45** (26.8 mg, 0.159 mmol), *N*,*N*-diethylpropane-1,3-diamine (38 μL, 0.24 mmol), K_3PO_4 (84.6 mg, 0.398 mmol) and dioxane (1.3 mL). Final product **22** was obtained as colorless oil (18 mg, 43 %). IR (ATR): 3266w, 2968m, 2933m, 2873m, 2831m, 1591s, 1518m, 1452m, 1375w, 1343w, 1166w, 1139w, 1067w, 801 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, δ): 8.06 (d, *J* = 5.6, H-C(2)), 6.26 (d, *J* = 5.6, H-C(3)), 5.94 (bs, H-N), 3.35-3.10 (m, 2H, -C*H*$_2$HN-), 2.90-2.70 (m, 2H), 2.65-2.45 (m, 6H), 2.40-2.25 (m, 2H), 1.95-1.65 (m, 6H), 1.03 (t, 3H, J = 7.0, -CH_2CH_3). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 155.41, 147.13, 115.32, 101.84, 52.74, 46.73, 43.64, 32.68, 25.27, 23.17, 22.72, 22.54, 11.38. HRMS: *m/z* 262.22666 corresponds to molecular formula $C_{16}H_{27}N_3H^+$ (error

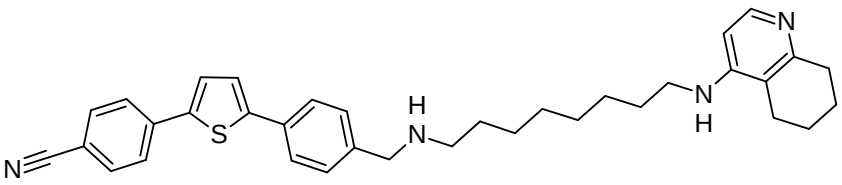
in ppm -4.25). HPLC purity (λ = 290 nm): method A: RT 1.353, area 96.66%; method E: RT 4.016, area 99.41%.

N^1,N^1-diethyl-N^4-(5,6,7,8-tetrahydroquinolin-4-yl)pentane-1,4-diamine (23).



Compound **23** was prepared by procedure E, using $Pd(OAc)_2$ (1.1 mg, 0.0049 mmol), SPhos (4.1 mg, 0.0010 mmol), **45** (21 mg, 0.12 mmol), N^1,N^1-diethylpentane-1,4-diamine (29.7 mg, 0.188 mmol), K_3PO_4 (66.5 mg, 0.312 mmol) and dioxane (1 mL). Final product **23** was obtained as colorless oil (9.9 mg, 27 %). IR (ATR): 3314w, 2967s, 2932s, 2865m, 2802m, 1589s, 1513m, 1452m,1371w, 1342w, 1165w, 805 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, δ): 8.07 (d, *J* = 5.6, H-C(2)), 6.32 (d, *J* = 5.6, H-C(3)), 3.85-3.70 (m, H-N), 3.65-3.47 (m, -C*H*-CH_3), 2.95-2.71 (m, 2H), 2.60-2.25 (m, 8H), 1.95-1.75 (m, 4H), 1.63-1.44 (m, 4H), 1.22 (d, 3H, *J* = 6.7, -CH-C*H*$_3$), 1.00 (t, 6H, J = 7.0, -CH_2C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 155.88, 150.68, 146.96, 114.97, 102.50, 52.75, 47.75, 46.79, 34.85, 32.75, 23.76, 22.79, 22.61, 22.52, 20.74, 11.56. HRMS: *m/z* 290.25771 corresponds to molecular formula $C_{18}H_{31}N_3H^+$ (error in ppm -4.69). HPLC purity (λ = 290 nm): method A: RT 8.644, area 97.25%; method E: RT 4.084, area 97.18%.

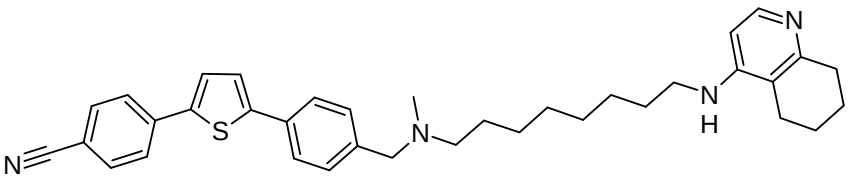
4-{5-[4-({[8-(5,6,7,8-tetrahydroquinolin-4-ylamino)octyl]amino}methyl)phenyl]-2-thienyl}benzonitrile (24).



Compound **24** was prepared by procedure D, using aldehyde 4-[5-(4-formylphenyl)thiophen-2-yl]benzonitrile[11] (61 mg, 0.21 mmol), amine **46** (87 mg, 0.32 mmol), glac. AcOH (19 μL, 0.32 mmol), $NaBH_4$ (47.9 mg, 1.27 mmol) and MeOH/ DCM (9 mL, 2:1, v/v). The product was purified using column chromatography (dry flash, silica-gel, eluent EtOAc/MeOH and flash, Biotage SP, NH column, eluent EtOAc/MeOH). Final product **24** was obtained as pale yellow solid (37 mg, 32%). M.p. = 155 – 157 ºC. IR (film): 3328m, 2930s, 2856s, 2869m, 2221m, 1701w, 1670w, 1653m, 1590s, 1524s, 1494m, 1452m, 1347m, 1310m, 1277m, 1166m, 1098w, 804m cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 8.07 (d, *J* = 5.7, H-C(2)), 7.74-7.53 (m, 6H, 4H-

ArCN and 2H-Ar), 7.45-7.28 (m, 4H, 2H-Ar and 2H-Thiophene), 6.30 (d, *J* = 5.7, H-C(3)), 3.80 (s, 2H, Ar*CH*$_2$-), 3.24-3.08 (m, 2H, ArNH*CH*$_2$-), 2.88-2.74 (m, 2H), 2.70-2.55 (m, 2H, ArCH$_2$NH*CH*$_2$-), 2.41-2.27 (m, 2H), 1.89-1.75 (m, 4H), 1.68-1.58 (m, 2H), 1.56-1.46 (m, 2H), 1.43-1.28(m, 8H, -(CH$_2$)$_4$-). ^{13}C NMR (125 MHz, CDCl$_3$, δ): 155.56, 151.54, 146.92, 145.99, 140.80, 138.53, 132.72, 132.34, 128.74, 126.06, 125.77, 125.64, 124.16, 118.84, 115.00, 110.37, 102.21, 53.68, 49.45, 42.96, 32.56, 30.08, 29.43, 29.27, 29.21, 27.24, 26.98, 22.69, 22.60, 22.48. HRMS: *m/z* 549.30216 corresponds to molecular formula $C_{35}H_{40}N_4SH^+$ (error in ppm -4.52). HPLC purity (λ = 330 nm): method A: RT 8.837, area 97.08%; method B: RT 7.689, area 95.53%.

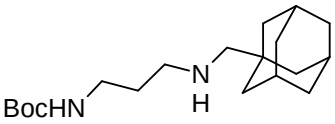
4-{5-[4-({methyl[8-(5,6,7,8-tetrahydroquinolin-4-ylamino)octyl]amino}methyl)phenyl]-2-thienyl}benzonitrile (25).



To a stirred solution of **24** (19 mg, 0.035 mmol) in methanol (0.9 mL) containing 37% aqueous formaldehyde (2.1 mg, 0.069 mmol), mixture of $ZnCl_2$ (9.4 mg, 0.069 mmol) and $NaBH_3CN$ (8.7 mg, 0.14 mmol) in methanol (0.9 mL) was added. The mixture was stirred at r. t. for 2h. The solvent was removed under reduced pressure. The residue was dissolved in DCM and 2M NH_3, organic layer was washed with brine and dried over anhydrous Na_2SO_4. The product was purified using column chromatography (flash, Biotage SP1, NH column, eluent MeOH). Final product **25** was obtained as pale yellow oil (16.4 mg, 84%). IR (film): 3267m, 3054m, 2928s, 2855s, 2225m, 1634s, 1600s, 1567s, 1537m, 1454m, 1374m, 1274m, 1175m, 1114w, 837m, 806m, 735m cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$, δ): 8.08 (d, *J* = 5.7, H-C(2)), 7.72-7.62 (m, 4H, H-ArCN), 7.60-7.55 (m, 2H, H-Ar), 7.41-7.27 (m, 4H, 2H-thiophene and 2H-Ar), 6.30 (d, *J* = 6.3, H-C(3)), 3.49 (s, 2H, Ar*CH*$_2$NH-), 3.20-3.10 (m, 2H), 2.89-2.75 (m, 2H), 2.43-2.27 (m, 4H), 2.20 (s, 3H, CH$_3$-), 1.90-1.78 (m, 4H), 1.68-1.58 (m, 4H), 1.57-1.47 (m, 2H), 1.43-1.28 (m, 8H, -(CH$_2$)$_4$-). ^{13}C NMR (125 MHz, CDCl$_3$, δ): 155.81, 151.40, 147.21, 146.07, 140.64, 139.70, 138.55, 132.72, 132.30, 129.61, 126.06, 125.63, 125.57, 124.12, 118.85, 114.97, 110.34, 102.22, 61.99, 57.48, 42.97, 42.31, 32.79, 29.42, 29.30, 29.23, 27.38, 27.29, 27.02, 22.72, 22.67, 22.54. HRMS: *m/z* 563.31839 corresponds to molecular formula $C_{36}H_{42}N_4SH^+$ (error in ppm -3.38).

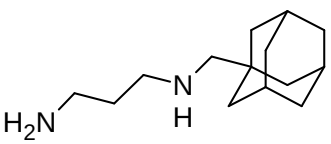
HPLC purity (λ = 330 nm): method A: RT 8.651, area 96.45%; method B: RT 7.691, area 95.11%.

***tert*-Butyl {3-[(1-adamantylmethyl)amino]propyl}carbamate (32).**



1-Adamantylmethanol (185.8 mg, 1.118 mmol) was dissolved in DCM (15 mL) followed by addition of PCC (361.3 mg, 1.676 mmol). The mixture was stirred at r.t. for 2h and filtered through SiO_2 column (eluent DCM) to afford the product. Adamantane-1-carbaldehyde was obtained as a white foam and used in the next step without characterization. Compound **32** was prepared by procedure D from **S1** (218.7 mg, 1.255 mmol) and adamantane-1-carbaldehyde (167.2 mg, 1.018 mmol) using glac. AcOH (0.09 mL, 1.6 mmol) and $NaBH_4$ (231.1 mg, 6.109 mmol). The product was purified using column chromatography (dry-flash, SiO_2, eluent DCM/MeOH gradient 4/6 → 2/8). Final product **32** was obtained as a pale yellow oil (134.8 mg, 37% for both steps). IR (ATR): 3345s, 3054w, 3007w, 2977m, 2904s, 2847m, 2782w, 2738w, 2658w, 1674s, 1538s, 1479m, 1450m, 1427w, 1390w, 1364m, 1341w, 1315w, 1281s, 1253m, 1227w, 1169m, 1114w, 1028w, 1000w, 948w, 897w, 866w, 800w, 781w, 754w, 719w, 654w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 6.06 (bs, H-NBoc), 3.22 (q, 2H, *J* = 5.2, -C*H*$_2$NHBoc), 2.69 (t, 2H, *J* = 6.0, -C*H*$_2$NHCH$_2$Ad), 2.23 (s, 2H, -NHC*H*$_2$Ad), 1.97 (bs, 3H, -Ad), 1.73-1.62 (m, 8H, -C*H*$_2$CH$_2$NHBoc, -Ad), 1.53 (d, 6H, *J* = 2.4, -Ad), 1.43 (s, 9H, -NHCOOC(C*H*$_3$)$_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 156.20, 78.56, 62.78, 49.70, 40.89, 40.45, 37.21, 33.31, 28.72, 28.46, 28.44. HRMS: *m/z* 323.26898 corresponds to molecular formula $C_{19}H_{34}N_2O_2H^+$ (error in ppm -1.01).

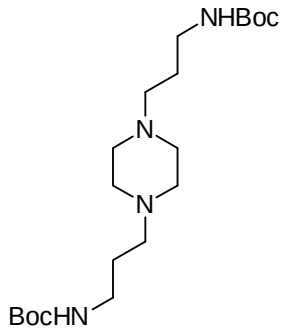
***N*-(1-adamantylmethyl)propane-1,3-diamine (33).**



Compound **33** was prepared from **32** (10.0 mg, 0.031 mmol) by procedure C. Final product **33** was obtained as a pale yellow oil (6.0 mg, 87%). IR (ATR): 3290w, 2900s, 2845s, 2676w, 1571w, 1475m, 1408w, 1364w, 1341w, 1315w, 1222w, 1152w, 1100w, 1002w, 814w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 2.76 (t, 2H, *J* = 6.9, -C*H*$_2$NH$_2$), 2.64 (t, 2H, *J* = 7.0, -C*H*$_2$NHCH$_2$Ad), 2.24 (s, 2H, -NHC*H*$_2$Ad), 1.96 (bs, 3H, -Ad), 1.73-1.60 (m, 8H, -C*H*$_2$CH$_2$NH$_2$, -Ad), 1.52 (d, 6H, *J* = 2.4, -Ad). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 63.12, 49.03, 40.95, 40.74, 37.24, 33.72, 33.34, 28.48.

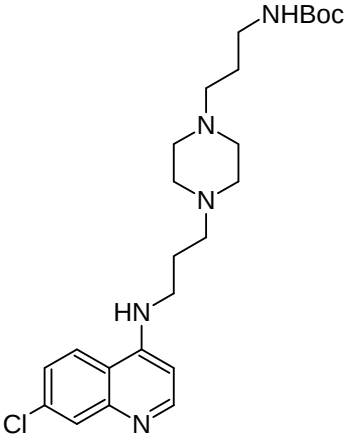
HRMS: *m/z* 223.21604 corresponds to molecular formula $C_{14}H_{26}N_2H^+$ (error in ppm - 3.73); *m/z* 112.11222 corresponds to molecular formula $C_{14}H_{26}N_2H_2^{2+}$ (error in ppm 1.28).

Di-*tert*-butyl [piperazine-1,4-diylbis(propane-3,1-diyl)]biscarbamate (35).



A 0.5 M solution of Boc_2O (2.12 g, 9.71 mmol) in DCM was added dropwise over 2 h to a 0.25 M solution of 1,4-bis(3-aminopropyl)piperazine **34** (4 mL, 19 mmol) in DCM cooled with an ice-bath. The reaction mixture was stirred overnight at r.t., filtered and then concentrated in vacuo. The resulting oil was dissolved in EtOAc, washed with with half-saturated brine, dried over $MgSO_4$ and solvent was evaporated under reduced pressure. Compound **35** was obtained after dry-flash chromatography: (SiO_2, eluent: DCM/MeOH(NH_3 satd) = 95/5) as a colorless solid (1.79 g, 46%); M.p. = 73-75 °C (hexane). IR (ATR): 3200m, 3008w, 2960m, 2869w, 2811m, 2744w, 2020w, 1712s, 1553m, 1457w, 1387w, 1362w, 1272m, 1169m, 1114w, 1084w, 1032w, 1005w, 972m, 888w, 856w, 819w, 764w, 733w, 693w cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 3.30-3.05 (m, 2H, -C*H*$_2$NHBoc), 2.75-2.25 (m, 12H, -C*H*$_2$N(CH$_2$CH$_2$)$_2$NC*H*$_2$-, -N(C*H*$_2$C*H*$_2$)$_2$N-), 1.85-1.55 (m, 2H, -C*H*$_2$CH$_2$NHBoc), 1.44 (s, 18H, -NHCOO-C(C*H*$_3$)$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): 156.04; 78.74; 56.84; 53.20; 39.97; 28.42; 26.30. HRMS: *m/z* 401.31137 corresponds to molecular formula $C_{15}H_{32}N_4O_2H^+$ (error in ppm -2.15).

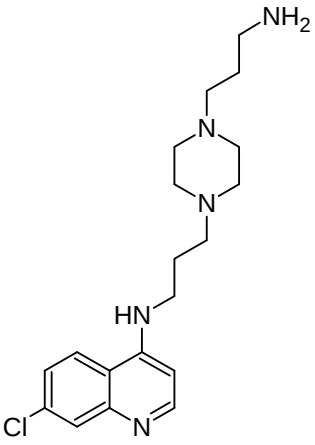
***Tert*-butyl [3-(4-{3-[(7-chloroquinolin-4-yl)amino]propyl}piperazin-1-yl)propyl]carbamate (36).**



A mixture of 4,7-dichloroquinoline (1.75 g, 17.7 mmol) and protected diaminoalkane **35** (5.32 g, 17.7 mmol) was gradually warmed to 80 °C over 1h with stirring and subsequently at 125 °C for 6-8 h. The reaction mixture was cooled to r.t. and taken up in DCM. The organic layer was washed with $NaHCO_3$ and finally with brine. The organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated under reduced pressure to get a final product. Compound **36** was obtained after dry-flash chromatography (SiO_2, eluent: DCM/MeOH(NH_3 satd) = 100/2) as

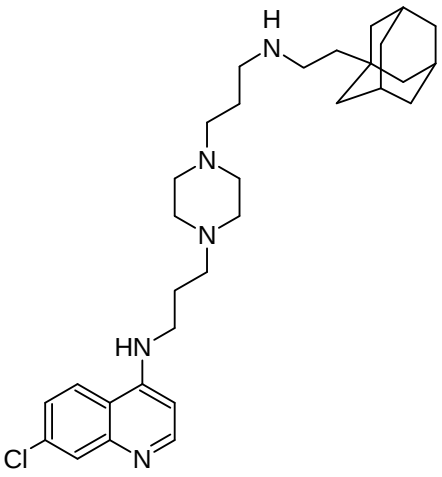
a colorless solid (4.0 g, 63%); M.p. = 148-150 °C (hexane). IR (ATR): 3215m, 3032w, 2943w, 2876w, 2807w, 2771w, 1709s, 1611w, 1582s, 1537m, 1487w, 1466w, 1447w, 1361w, 1333w, 1308w, 1274m, 1252w, 1170m, 1149m, 1137m, 1102w, 1078w, 1063w, 1032w, 987w, 974w, 947w, 890w, 880w, 856w, 838w, 812w, 764w, 710w, 652w, 599w, 503w, 425w cm^{-1}. ^1H NMR (200 MHz, $CDCl_3/CD_3OD$): 8.40 (d, 1H, *J* = 5.6 Hz, H-C(2)), 7.95-7.80 (m, 2H, H-C(8) and H-C(5)), 7.40-7.25 (m, 1H, H-C(6)), 6.34 (d, 1H, *J* = 5.6 Hz, H-C(3)), 3.50-3.30 (m, 2H, ArNHCH_2-), 3.30-3.10 (m, 2H, -CH_2NHBoc), 3.00-2.30 (m, 12H, -CH_2N(CH_2CH_2)$_2$NCH_2-, -N(CH_2CH_2)$_2$N-), 2.10-1.80 (m, 2H, ArNHCH$_2$CH_2-), 1.80-1.60 (m, 2H, -CH_2CH$_2$NHBoc), 1.46 (s, 9H, -NHCOO-C(CH_3)$_3$). ^{13}C NMR (50 MHz, $CDCl_3/CH_3OD$): 156.26; 151.34; 150.68; 148.26; 134.84; 127.38; 124.68; 122.26; 117.11; 98.21; 78.93; 57.81; 57.56; 56.37; 53.22; 53.02; 52.89; 43.04; 39.07; 28.15; 26.22; 23.54. HRMS: *m/z* 462.26263 corresponds to molecular formula $C_{24}H_{36}ClN_5O_2H^+$ (error in ppm -0.87). ($C_{24}H_{36}ClN_5O_2\times1/3H_2O$) Calcd: C, 61.59; H, 7.90; N, 14.96. Found: C, 61.46; H, 7.75; N, 15.23.

***N*-{3-[4-(3-aminopropyl)piperazin-1-yl]propyl}-7-chloroquinolin-4-amine (37).**



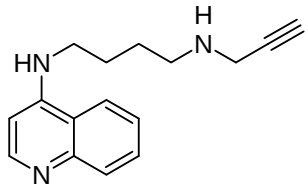
Compound **37** was prepared from **36** (500 mg, 1 mmol) by procedure C and was obtained as a yellow powder (348 mg, 89%), softenes at 80-82°C. IR (ATR): 3234m, 3060w, 2934m, 2816m, 1610w, 1578s, 1538m, 1489w, 1463w, 1447w, 1433w, 1403w, 1368m, 1331m, 1283w, 1255w, 1201w, 1136m, 1112w, 1080w, 1033w, 999w, 904w, 878w, 854w, 819w, 806w, 764w, 730w, 649w, 621w, 598w, 539w, 494w, 430w cm^{-1}. ^1H NMR (200 MHz, $CDCl_3/CD_3OD$): 8.40 (d, 1H, *J* = 5.6 Hz, H-C(2)), 8.00-7.80 (m, 2H, H-C(8), H-C(5)), 7.50-7.40 (br s, 1H, -N*H*), 7.29 (dd, 1H, *J* = 2.4 Hz, *J* = 9.0 Hz, H-C(6)), 6.30 (d, 1H, *J* = 5.6 Hz, H-C(3)), 3.50-3.20 (m, 2H, ArNHCH_2-), 3.10-2.90 (m, 2H, -CH_2NH$_2$), 2.90-2.40 (s, 12H, -CH_2N(CH_2CH_2)$_2$NCH_2-, -N(CH_2CH_2)$_2$N-), 2.10-1.80 (m, 2H, ArNHCH$_2$CH_2-), 1.80-1.60 (m, 2H, -CH_2CH$_2$NH$_2$). ^{13}C NMR (50 MHz, $CDCl_3/CD_3OD$): 151.40; 150.63; 148.28; 134.63; 127.43; 124.52; 122.30; 117.13; 98.16; 57.56; 56.24; 52.93; 43.06; 40.00; 29.35; 23.34. HRMS: *m/z* 362.20995 corresponds to molecular formula $C_{19}H_{28}ClN_5H^+$ (error in ppm -1.80).

***N*-{3-[4-(3-{[2-(1-Adamantyl)ethyl]amino}propyl)piperazin-1-yl]propyl}-7-chloroquinolin-4-amine (38).**



Compound **38** was prepared from amine **37** (137 mg, 0.38 mmol) and adamantane-1-acetaldehyde (68 mg, 0.38 mmol) using $NaBH(OAc)_3$ (161 mg, 0.76 mmol) by procedure D and was obtained after dry-flash chromatography (SiO_2, eluent: DCM/MeOH(NH_3 satd) = 100/2) and flash chromatography (Biotage SP1 RP column, gradient: MeOH/H_2O = 8/1→95/5) as a colorless foam (108 mg, 54%) softenes at 120-122 °C. IR (ATR): 3235m, 2899s, 2841m, 2806m, 1610w, 1586s, 1540m, 1486w, 1446m, 1368w, 1353w, 1332w, 1307w, 1283w, 1242w, 1198w, 1140m, 1074w, 1016w, 987m, 958m, 898w, 875w, 856w, 836w, 812m, 793, 759w, 728m, 596m, 501m, 428w cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): 8.50 (d, 1H, *J* = 5.0 Hz, H-C(2)), 8.00-7.80 (m, 2H, H-C(8), H-C(5)), 7.58 (br s, 1H, -N*H*), 7.30 (dd, 1H, *J* = 1.9 Hz, *J* = 9.0 Hz, H-C(6)), 6.30 (d, 1H, *J* = 5.6 Hz, H-C(3)), 3.45-3.25 (m, 2H, ArNHCH_2-), 3,00-2,20 (m, 16H, -CH_2NHCH$_2$CH$_2$Ad, -CH_2CH$_2$Ad, -N(CH_2CH_2)$_2$N-, -CH_2 N(CH$_2$CH$_2$)$_2$NCH_2-), 2.10-1.40 (m, 19H, ArNHCH$_2$CH_2-, -CH_2CH$_2$NHCH$_2$CH$_2$Ad, -Ad), 1.40-1.35 (m, 2H, -CH_2Ad). ^{13}C NMR (50 MHz, $CDCl_3$): 152.12; 150.54; 148.99; 134.54; 128.44; 124.54; 122.43; 117.40; 98.38; 58.74; 57.25; 53.46; 53.28; 48.72; 44.17; 42.50; 37.00; 31.76; 28.51; 26.51; 23.27. Anal. ($C_{31}H_{46}ClN_5 \times 3/2H_2O$) Calcd: C, 67.55; H, 8.96; N, 12.71. Found: C, 67.86; H, 9.22; N, 12.89.

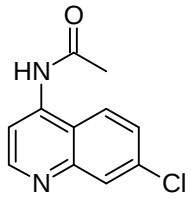
***N*-(prop-2-yn-1-yl)-*N*'-(quinolin-4-yl)butane-1,4-diamine (41).**



According to the procedure described in literature[12], **AQ8**[7] (203.6 mg, 0.9457 mmol) was dissolved in $EtOH_{aps}$ (10 mL), K_2CO_3 was added (130.7 mg, 0.9457 mmol), and then propargyl bromide (36 μL, 0.47 mmol). The mixture was stirred at r.t. for 24 h. Solvent was evaporated under the reduced pressure, and crude product was purified using column chromatography (dry-flash, SiO_2, eluent DCM, DCM/MeOH gradient 7/3 → 3/7). Final product **41** was obtained as colorless oil (59 mg, 49%). IR (ATR): 3287m, 3066m, 2931m, 2856m, 1617w, 1579s, 1540m, 1457w, 1438w, 1395w, 1373w, 1339m, 1281w, 1251w, 1225w, 1170w,

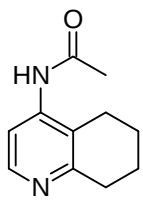
1127w, 1036w, 867w, 808w, 763m, 651w cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, δ): 8.54 (d, *J* = 5.6, H-C(2)), 8.01-7.93 (m, H-C(8)), 7.82-7.75 (m, H-C(5)), 7.66-7.55 (m, H-C(7)), 7.45-7.34 (m, H-C(6)), 6.38 (d, *J* = 5.6, H-C(3)), 5.88-5.74 (m, *H*-N), 3.46-3.43 (m, 2H, -C*H*$_2$C≡CH), 3.36-3.23 (m, 2H, ArNHC*H*$_2$-), 2.82-2.72 (m, 2H, ArNHCH$_2$CH$_2$CH$_2$C*H*$_2$-), 2.27-2.20 (m, 1H, -C≡C*H*), 1.93-1.77 (m, 2H, ArNHCH$_2$C*H*$_2$-), 1.75-1.59 (m, 2H, ArNHCH$_2$CH$_2$C*H*$_2$-). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 151.01, 149.85, 148.37, 129.74, 128.85, 124.37, 119.64, 118.80, 98.50, 81.82, 71.50, 47.85, 43.01, 38.05, 27.39, 26.24. HRMS: *m/z* 254.16429 corresponds to molecular formula $C_{16}H_{19}N_3H^+$ (error in ppm -3.47).

_N_-(7-chloroquinolin-4-yl)acetamide (42).[10]



A solution of **S2** (844 mg, 4.73 mmol) in acetic anhydride (3.4 mL) was refluxed for 2h. After cooling to r.t. brine and 10% aqueous NaOH were added. The mixture was extracted with ethyl acetate and organic extracts were dried over anh. Na_2SO_4. The product was purified using column chromatography (dry-flash, SiO_2, eluent EtOAc/MeOH and flash, Biotage SP1, RP column, eluent MeOH/H_2O). Final product **42** was obtained as white solid (799 mg, 91 %). M.p. = 169 – 172 ºC. IR (KBr): 3434s, 3267s, 3048m, 2924m, 2852m, 1662s, 1614s, 1594m, 1570s, 1528s, 1491s, 1444m, 1422m, 1384m, 1371m, 1311s, 1274m, 1244m, 1187w, 1167w, 1104w, 1081w, 1041w, 1016w, 959w, 970w, 918w, 854m, 833m, 818m, 765w, 714m, 668w, 636w, 615w, 587w, 557w, 519w, 502w, 474w, 433w, 420w, 403w cm^{-1}. ^1H NMR (500 MHz, CD_3OD, δ): 8.79-8.68 (m, H-C(2)), 8.26-8.19 (m, H-C(5)), 8.18-8.11 (m, H-C(8)), 8.30-7.92 (m, H-C(3)), 2.33 (s, 3H, C*H*$_3$-). ^{13}C NMR (125 MHz, CD_3OD, δ): 172.74, 153.10, 150.25, 144.14, 137.05, 128.55, 128.39, 124.95, 121.12, 113.90, 24.30. HRMS: *m/z* 221.04691 corresponds to molecular formula $C_{11}H_9ClN_2OH^+$ (error in ppm -3.19).

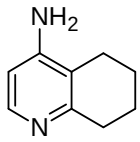
_N_-(5,6,7,8-tetrahydroquinolin-4-yl)acetamide (43).



Compound **42** (551 mg, 2.49 mmol) was hydrogenated using PtO_2 (55 mg, 10 wt. %) as catalyst under hydrogen (50 psi) in glac. AcOH (48 mL) and perchloric acid (0.3 mL). The mixture was shaken at r.t. for 64 h. The catalyst was filtered off, 10% NaOH in water was added to filtrate, extracted with DCM and dried over anh. Na_2SO_4. The product was purified using column chromatography (dry-flash, SiO_2, eluent

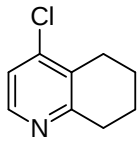
EtOAc/MeOH). Final product **43** was obtained as white solid (310 mg, 65 %). M.p. = 148 – 151 ºC. IR (ATR): 3352m, 3147m, 3069m, 2934s, 2860m, 1702s, 1682s, 1583s, 1514s, 1459m, 1435m, 1406m, 1369m, 1337m, 1297s, 1254m, 1166w, 1002w, 845w, 736w cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD, δ): 8.17 (d, *J* = 5.5, H-C(2)), 7.72 (d, *J* = 5.5, H-C(3)), 2.92-2.82 (m, 2H, H-C(8)), 2.72-2.65 (m, 2H, H-C(5)), 2.20 (s, 3H, C*H*$_3$), 1.91-1.79 (m, 4H, H-C(6) and H-C(7)). ^{13}C NMR (125 MHz, CD_3OD, δ): 172.45, 158.64, 146.69, 146.37, 125.22, 116.29, 33.14, 24.81, 24.00, 23.47, 23.41. HRMS: *m/z* 191.11758 corresponds to molecular formula $C_{11}H_{14}N_2OH^+$ (error in ppm -1.64).

5,6,7,8-Tetrahydroquinolin-4-amine (44).



The solution of **43** in 2M HCl was stirred for 3 h at 70 °C. After cooling to r. t., ammonia was added. The mixture was extracted with DCM and dried over anh. Na_2SO_4. Final product **44** was obtained after evaporation of organic layer as pale yellow solid (182 mg, 89 %). M.p. = 125 – 126 ºC. IR (ATR): 3336s, 3194s, 2933s, 2860m, 1637s, 1590s, 1481m, 1451m, 1351m, 1274w, 1190w, 1164w, 1102w, 899w, 818m, 736 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.02 (d, *J* = 5.5, H-C(2)), 6.38 (d, *J* = 5.5, H-C(3)), 4.05 (bs, NH_2), 2.95-2.73 (m, 2H, H-C(5)), 2.59-2.33 (m, 2H, H-C(8)), 2.10-1.76 (m, 4H, H-C(6) and H-C(7)). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 157.03, 150.83, 146.74, 115.84, 107.10, 32.71, 22.87, 22.75, 22.48. HRMS: *m/z* 149.10661 corresponds to molecular formula $C_9H_{12}N_2H^+$ (error in ppm -4.78).

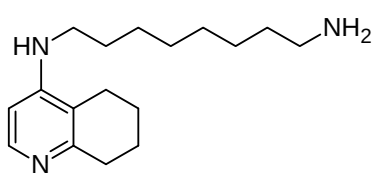
4-Chloro-5,6,7,8-tetrahydroquinoline (45).



To a stirring solution of **44** (380 mg, 2.6 mmol) in glac. AcOH (2.3 mL) at 0 °C, 28% HCl (1.5 mL) and aqueous solution of $NaNO_2$ (257 mg, 0.85 mL) were added dropwise, respectively. After 10 minutes at 0 °C, resulting mixture was added dropwise to a solution of CuCl (659 mg, 6.66 mmol) in 28 % HCl (1.2 mL) at same temperature. The stirring was continued at r. t. After 17 h, solution of NaOH in water was added and extracted with DCM. Organic layer was dried over anh. Na_2SO_4. The crude product was purified using colum chromatography (dry-flash, SiO_2, eluent EtOAc/MeOH). Final product **45** was obtained as a coroless oil (226 mg, 53%). IR (ATR): 3041w, 2937s, 2863s, 1734w, 1674w, 1553s, 1451s, 1432m, 1400s, 1332w, 1230w, 1194w, 1161w, 1082w, 1061w, 953w, 834m, 787m, 672w cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7,77-7,65 (m, H-C(2)), 7,58-7,48 (m, H-C(3)), 1,88-1,20 (m, 8H, H-C(5), H-C(6), H-C(7) and H-C(8)). GC/MS (m/z (%)): 165.9 ([M^+], 100); 132.0 (33).

N^1-(5,6,7,8-tetrahydroquinolin-4-yl)octane-1,8-diamine (46).



Compound **46** was prepared by procedure E, using $Pd(OAc)_2$ (9.9 mg, 0.044 mmol), SPhos (36.3 mg, 0.0883 mmol), **45** (185 mg, 1.10 mmol), 1,8-diaminooctane (239 mg, 1.66 mmol), K_3PO_4 (587 mg, 2.76 mmol) and dioxane (9.3 mL). Final product **46** was obtained as colorless oil (200 mg, 66%). IR (ATR): 3299m, 2928s, 2855s, 1592s, 1523m, 1456m, 1344m, 1165w, 808 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.08 (d, J = 5.7, H-C(2)), 6.31 (d, J = 5.7, H-C(3)), 3.93 (s, H-N, exchangable with D_2O), 3.25 – 3.05 (m, 2H), 2.90 – 2.75 (m, 2H), 2.68 (t, J = 7.0, 2H), 2.41 – 2.26 (m, 2H), 1.94 – 1.76 (m, 4H), 1.74 – 1.54 (m, 4H), 1.50 – 1.25 (m, 8H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 155.72, 151.44, 147.10, 114.97, 102.21, 42.95, 42.19, 33.75, 32.71, 29.37, 29.31, 29.21, 26.99, 26.79, 22.70, 22.64, 22.50. HRMS: *m/z* 276.24282 corresponds to molecular formula $C_{17}H_{29}N_3H^+$ (error in ppm -2.19).

Table S1. *In vitro* activities against *L. infantum* and *L. tropica* promastigotes and cytotoxicity against THP-1 human cells[a]

Comp.	L. *infantum* IC_{50} (μM)[b]	L. *tropica* IC_{50} (μM)[b]	THP-1 IC_{50} (μM)[c]	SI (THP/ *L.i.*)[d]	SI (THP/ *L.t.*)[d]	Ref. of comp.[e]
1	8.67	2.77	23.66	2.7	8.5	new
2	6.49	2.96	>109.6	>16.9	>37.0	new
3	16.60	9.35	>65.2	>3.9	>7.0	new
4	16.60	6.63	>59.7	>3.6	>9.0	new
5	1.91	2.24	12.59	6.6	5.6	new
6	1.77	1.30	6.39	3.6	4.9	new
7	0.73	0.66	1.81	2.5	2.7	14
8	2.46	1.84	3.29	1.3	1.8	14
9	2.40	2.35	4.90	2.0	2.1	14
10	0.52	0.51	1.00	1.9	2.0	new
11	1.14	1.31	2.96	2.6	2.3	7
12	0.64	0.68	3.76	5.8	5.5	7
13	1.23	1.24	4.25	3.4	3.4	7
14	0.51	0.50	1.91	3.8	3.8	7
15	0.48	0.43	4.73	9.9	10.9	new
16	1.03	0.81	2.31	2.2	2.8	11
17	1.02	0.85	4.28	4.2	5.0	13
18	1.24	1.02	2.35	1.9	2.3	15
19	0.98	0.91	2.44	2.5	2.7	11
20	1.55	1.22	2.79	1.8	2.3	11
21	1.02	1.37	7.11	7.0	5.2	new
22	>76.5	>76.5	>76.5	>1	>1	new
23	>69.1	>69.1	>69.1	>1	>1	new
24	0.72	0.75	2.31	3.2	3.1	new
25	0.83	0.80	3.68	4.4	4.6	new
26	2.30	1.94	5.01	2.2	2.6	11
27	1.22	1.54	2.80	2.3	1.8	11
28	5.42	7.11	8.10	1.5	1.1	11
29	0.35	0.30	1.38	4.0	4.6	11
30	0.80	1.06	3.85	4.8	3.6	11
Control[f]	0.13	0.14	>10.8	>83.1	>77.1	/

[a]Antileishmanial IC_{50} values against promastigote stages (μM), MTT assay; [b]All *in vitro* experiments were performed in duplicate, mean values are given; [c]Cytotoxicity against differentiated THP-1, human monocytic cell line derived from an acute monocytic leukemia patient. [d]Selectivity index; [e]The syntheses of compounds are presented in our previous papers[7,11,13,14,15]. [f]Control drug: amphotericin B

Table S2. *In vitro* activities against intramacrophage *L. infantum* amastigotes

Compound	*In Vitro* Antiamastigote Activity at 0.5 µM[a]	*In Vitro* Antiamastigote Activity IC_{50} (µM)[b]	THP-1[c] IC_{50} (µM)	SI (THP/IPT)[d]
1	8.9		23.7	
2	0.2		>109.6	
3	18.3		>65.2	
4	0		>59.7	
5	13.9		12.6	
6	23.3		6.40	
7	15.8		1.80	
8	**29.6**	**1.91**	**3.29**	**1.72**
9	22		4.90	
10	**72.2**	**0.31**	**1.00**	**3.22**
11	**26.4**	**1.85**	**2.96**	**1.60**
12	0		3.76	
13	**38.9**	**1.29**	**4.25**	**3.29**
14	**26.4**	**>1**	**1.91**	**< 1.91**
15	**47.6**	**0.58**	**4.73**	**8.15**
16	10.4		2.31	
17	14.4		4.28	
18	**42.7**	**0.65**	**2.35**	**3.61**
19	**36.9**	**0.73**	**2.44**	**3.34**
20	**42.2**	**0.79**	**2.79**	**3.51**
21	21		7.11	
22	1.1		>76.5	
23	11.8		>69.1	
24	**29.6**	**>1**	**2.31**	**< 2.3**
25	20.5		3.68	
26	2.4		5.01	
27	12.7		2.80	
28	13.8		8.10	
29	13.5		1.38	
30	23.6		3.85	
Control[e]	95.5	0.21	>10.8	>51.4

[a]Mean value of two or three experiments. [b]Mean value of two experiments. [c]Cytotoxicity against differentiated THP-1, human monocytic cell line derived from an acute monocytic leukemia patient. [d]Selectivity Index (IC_{50} against THP-1/IC_{50} against intracellular amastigotes); [e]Control drug: amphotericin B.

Table S3. Antileishmanial activity *in vivo*.

Control (PBS)	**Liver weight in mg (W)**	**Amastigotes/Liver cell (A/C)**	**Relative load W x A/C**
1	930	40/503	74.0
2	1000	44/502	87.6
3	700	49/507	67.6
4	630	35/506	43.6
5	622	47/500	58.5
Mean			**66.3**

Comp. 10 (100mg/kg × 4 days, p.o.)	**Liver weight in mg (W)**	**Amastigotes/Liver cell (A/C)**	**Relative load W x A/C**
1	672	0/500	0
2	636	0/500	0
3	798	0/500	0
Mean			**0**
Reduction from control (%)			**100**

Note: signs of toxicity; 1 mouse died on D10; 1 mouse died on D12

Comp. 10 (60mg/kg × 4 days, p.o.)	**Liver weight in mg (W)**	**Amastigotes/Liver cell (A/C)**	**Relative load W x A/C**
1	655	2/505	2.6
2	482	2/500	1.9
3	653	3/507	3.9
4	753	1/500	1.5
5	756	2/503	3.0
Mean			**2.6**
Reduction from control (%)			**96.1**

Comp. 10 (10mg/kg × 4 days, s.c.)	**Liver weight in mg (W)**	**Amastigotes/Liver cell (A/C)**	**Relative load W x A/C**
1	575	10/500	11.5
2	544	12/510	12.8
3	666	12/507	15.7
4	528	9/500	9.5
5	609	10/508	12.0
Mean			**12.3**
Reduction from control (%)			**81.4**

Comp. 15 (100mg/kg × 4 days, p.o.)	**Liver weight in mg (W)**	**Amastigotes/Liver cell (A/C)**	**Relative load W x A/C**
1	638	1/500	1.3
2	630	2/503	2.5
3	747	0/500	0
4	830	0/508	0
5	513	0/503	0
Mean			**0.76**

Reduction from control (%)			**98.8**

Comp. 15 (50mg/kg × 4 days, p.o.)	**Liver weight in mg (W)**	**Amastigotes/Liver cell (A/C)**	**Relative load W x A/C**
1	838	2/506	3.3
2	730	2/510	2.9
3	695	3/500	4.2
4	725	2/502	2.9
5	572	3/503	3.4
Mean			3.3
Reduction from control (%)			**95.0**

Table S4. Antileishmanial activity *in vivo*.

Control (PBS)	**Liver weight in mg (W)**	**Amastigotes/Liver cell (A/C)**	**Relative load W x A/C**
1	720	50/503	71.6
2	820	56/500	91.8
3	950	48/513	90.7
4	570	50/548	52.0
5	510	46/500	46.9
Mean relative load			**70.6**

Comp. 10 (5mg/kg × 5 days, s.c.)	**Liver weight in mg (W)**	**Amastigotes/Liver cell (A/C)**	**Relative load W x A/C**
1	680	24/500	32.6
2	780	20/510	30.6
3	750	18/500	27.0
4	720	25/500	36.0
5	600	22/515	25.6
Mean relative load			**30.4**
Reduction from control (%)			**56.9**

Comp. 15 (10mg/kg × 5 days, s.c.)	**Liver weight in mg (W)**	**Amastigotes/Liver cell (A/C)**	**Relative load W x A/C**
1	920	22/500	40.5
2	720	23/510	32.5
3	810	23/500	37.3
4	890	21/520	35.9
5	740	25/515	35.9
Mean relative load			**36.4**
Reduction from control (%)			**48.4**

Comp. 15 (5mg/kg × 5 days, s.c.)	**Liver weight in mg (W)**	**Amastigotes/Liver cell (A/C)**	**Relative load W x A/C**
1	1080	28/500	60.5
2	830	30/510	48.8
3	680	38/500	51.7

4	600	40/500	48.0
5	570	38/500	43.3
Mean relative load			**50.5**
Reduction from control (%)			**28.5**

Comp. 15 (1mg/kg × 5 days, s.c.)	**Liver weight in mg (W)**	**Amastigotes/Liver cell (A/C)**	**Relative load W x A/C**
1	670	44/506	58.3
2	780	42/510	64.2
3	600	45/500	54.0
4	800	43/500	68.8
5	500	44/500	44.0
Mean relative load			**57.9**
Reduction from control (%)			**18.0**

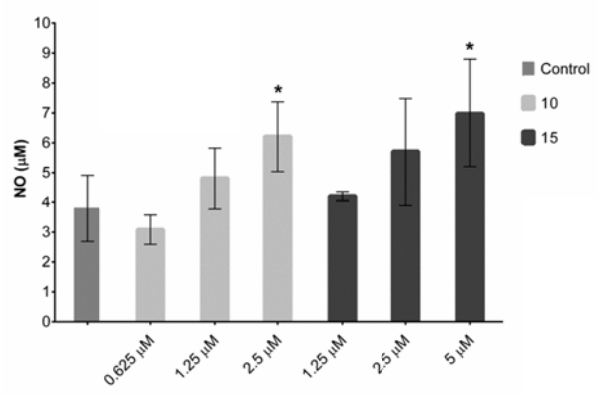


Figure S1. Nitric oxide production by BMDM treated with **10** or **15**. BMDM were primed with IFN-γ for 2 h, and then treated with different concentrations of **10** or **15**. Levels of nitrite were measured into the supernatants after 24h by Griess assay. Data are the mean ± SD of three independent experiments in triplicate. *p < 0.01 versus control

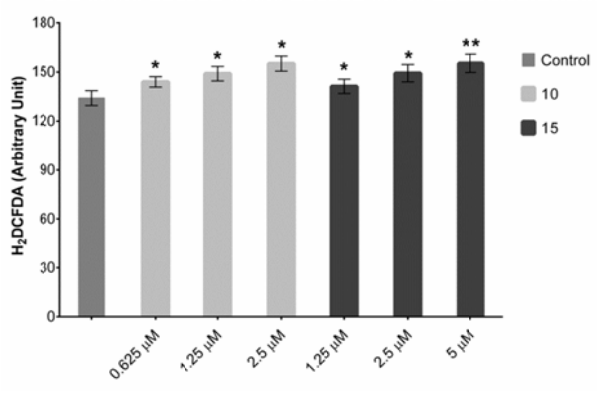


Figure S2. ROS production by BMDM treated with **10** or **15**. BMDM were primed with IFN-γ for 2 h, and then treated with different concentrations of **10** or **15**. Levels of ROS were measured into the supernatants after 24h by H_2DCFDA. Data are the mean ± SD of three independent experiments in triplicate. *p < 0.01 versus control; **p < 0.001 versus control

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Supporting Information - II

Novel aminoquinoline derivatives significantly reduce parasite load in *Leishmania infantum* infected mice

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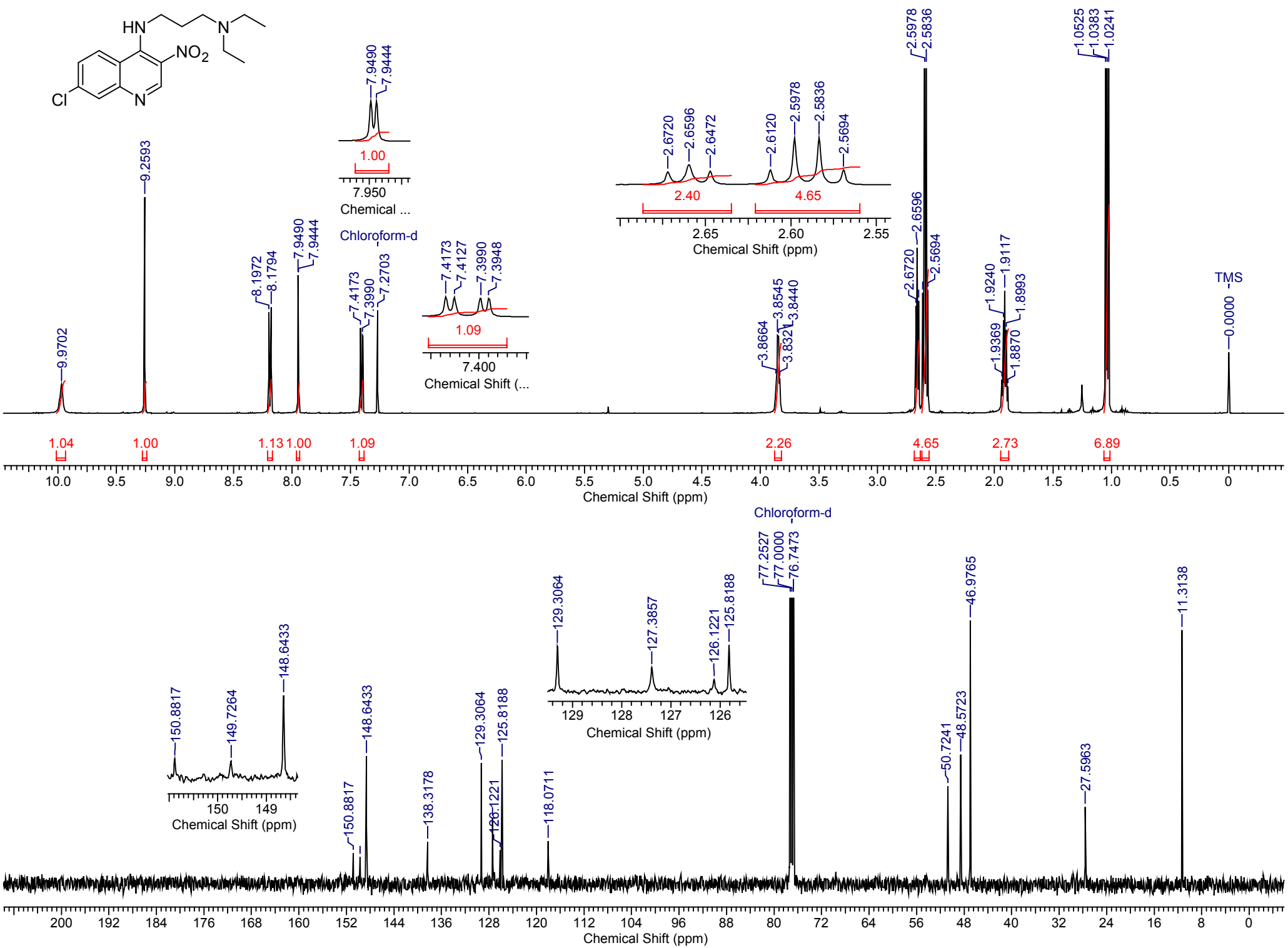
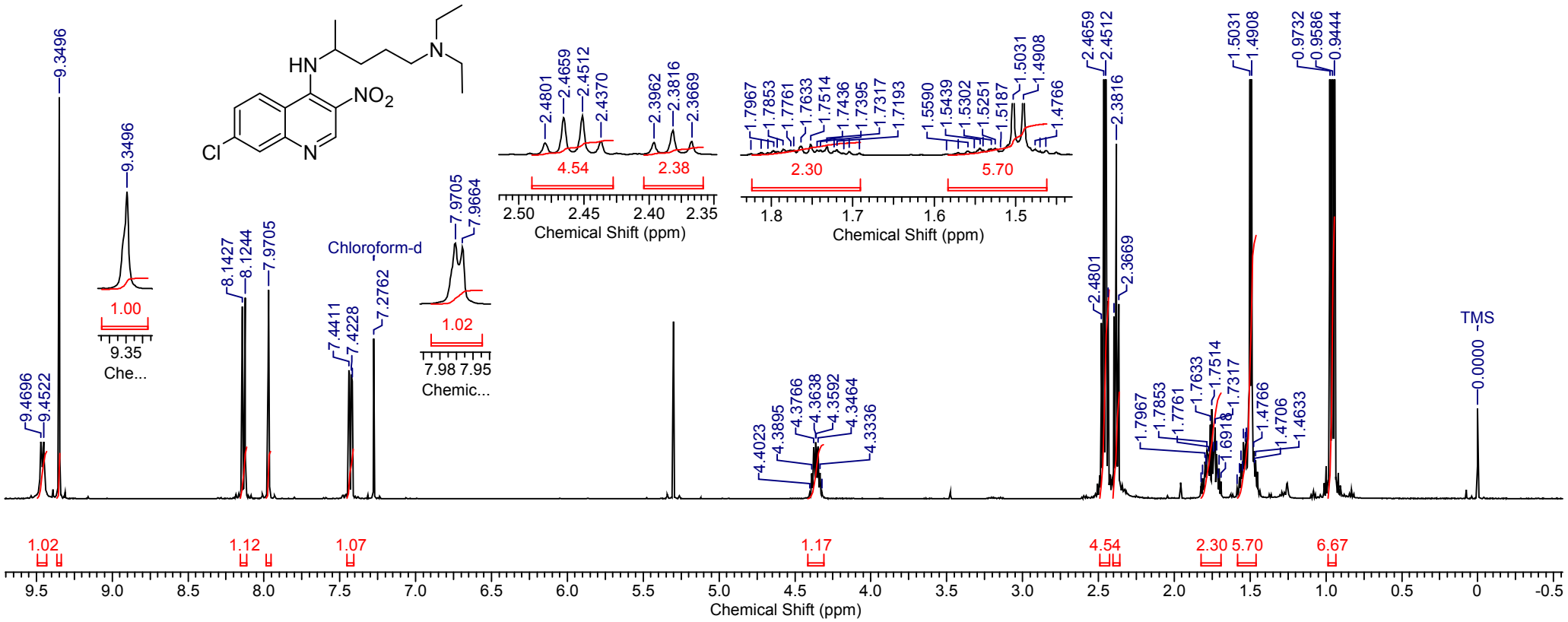
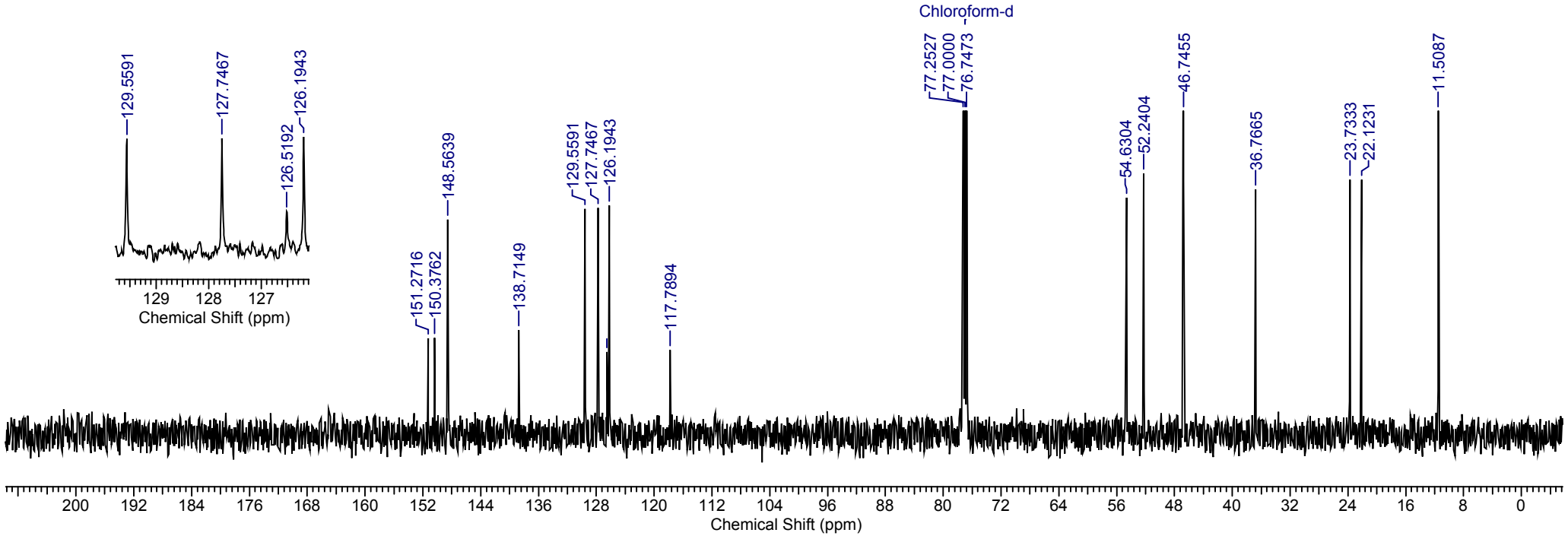
NMR spectra of synthesized compounds

***N'*-(7-chloro-3-nitroquinolin-4-yl)-*N*,*N*-diethylpropane-1,3-diamine (1)**



N_4-(7-chloro-3-nitroquinolin-4-yl)-N_1,N_1-diethylpentane-1,4-diamine (2)





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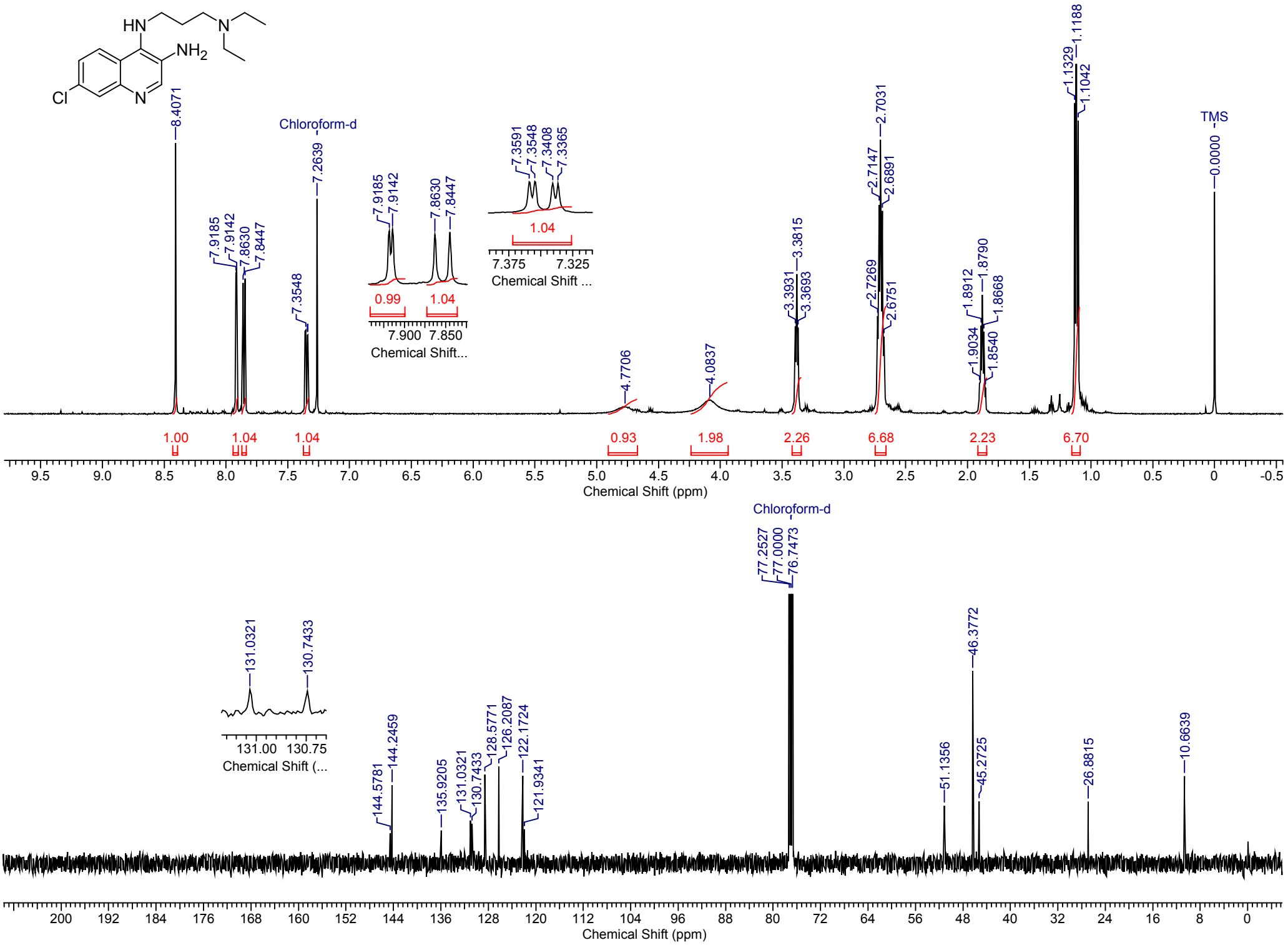

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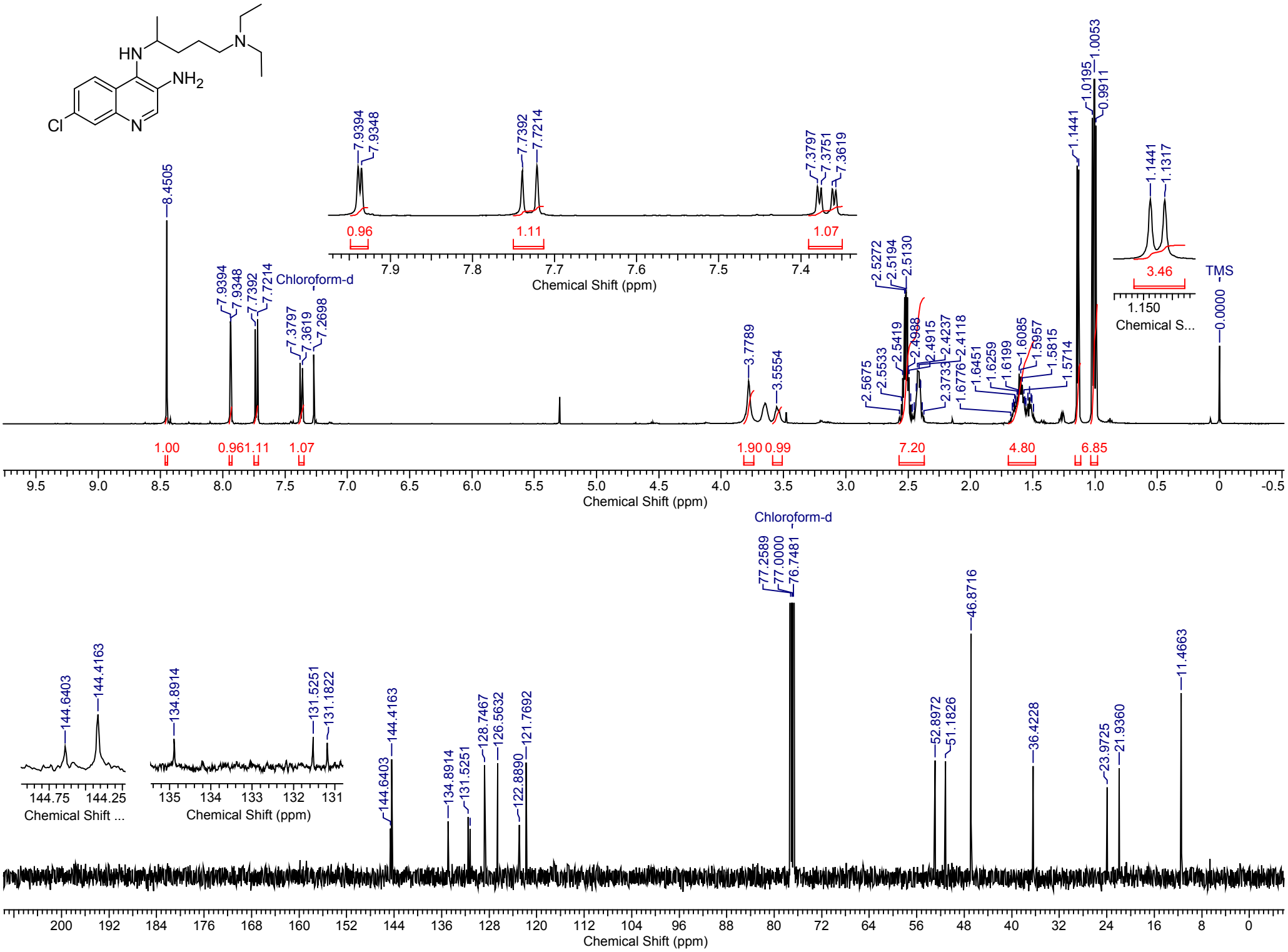

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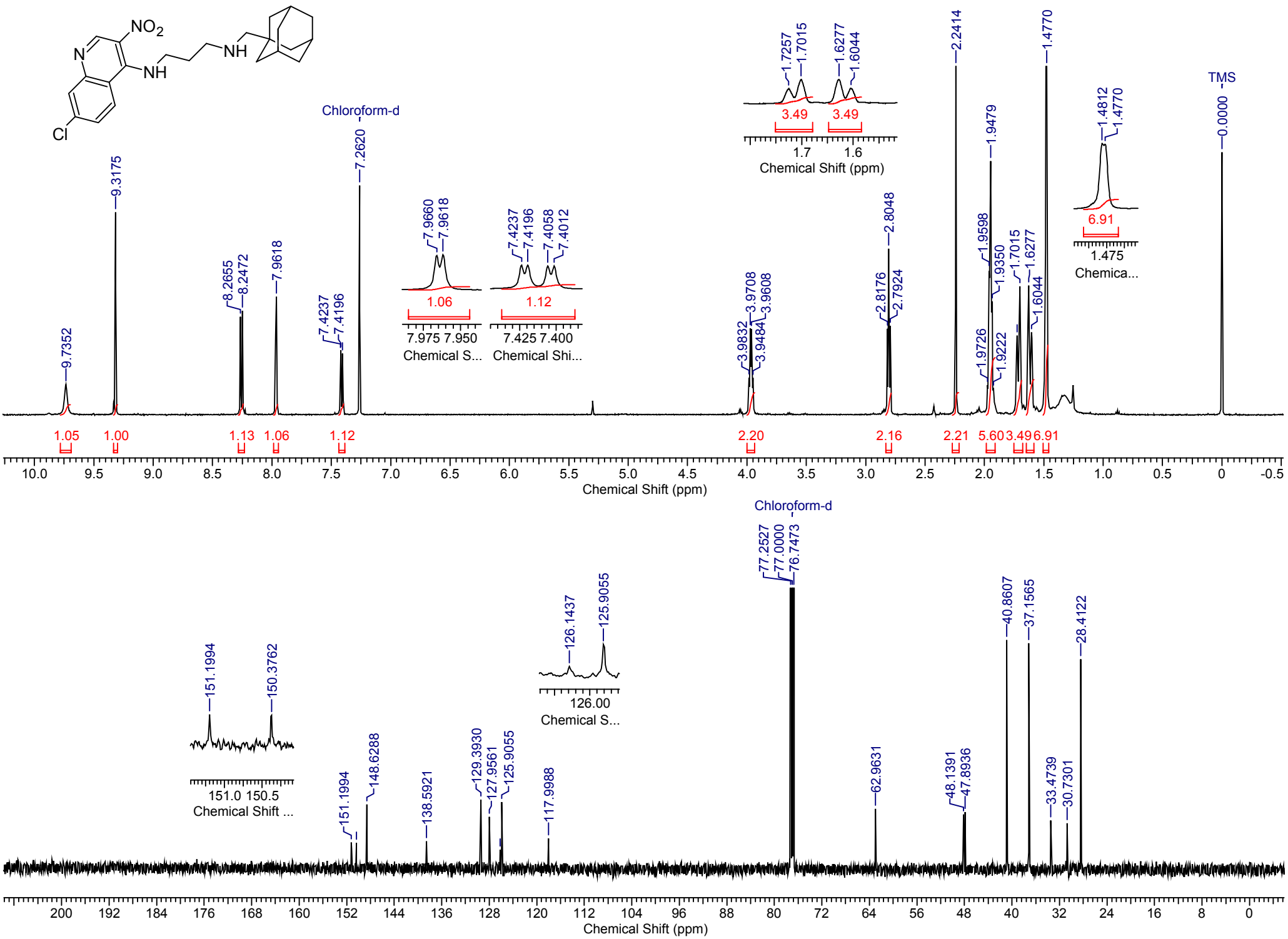

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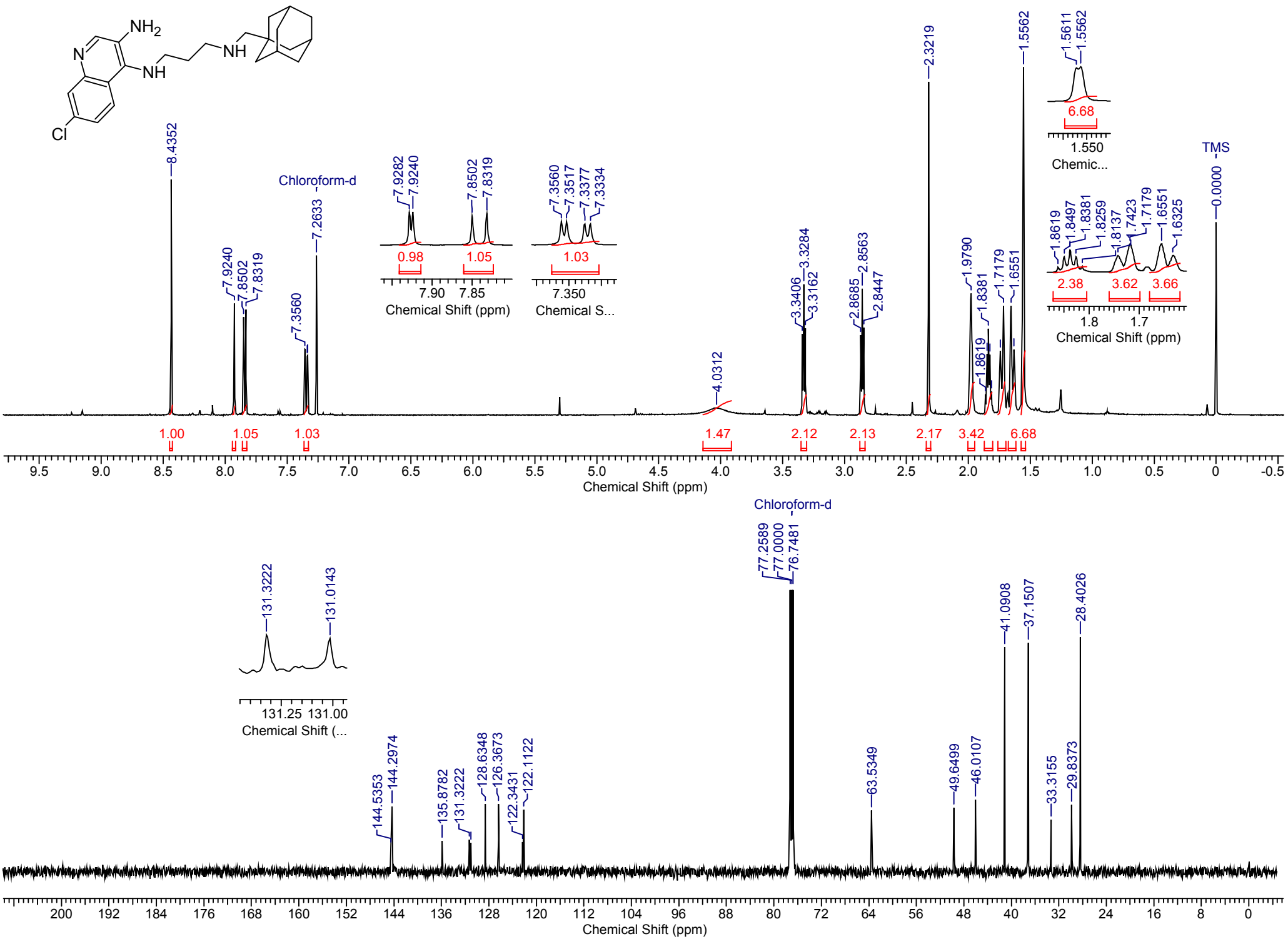

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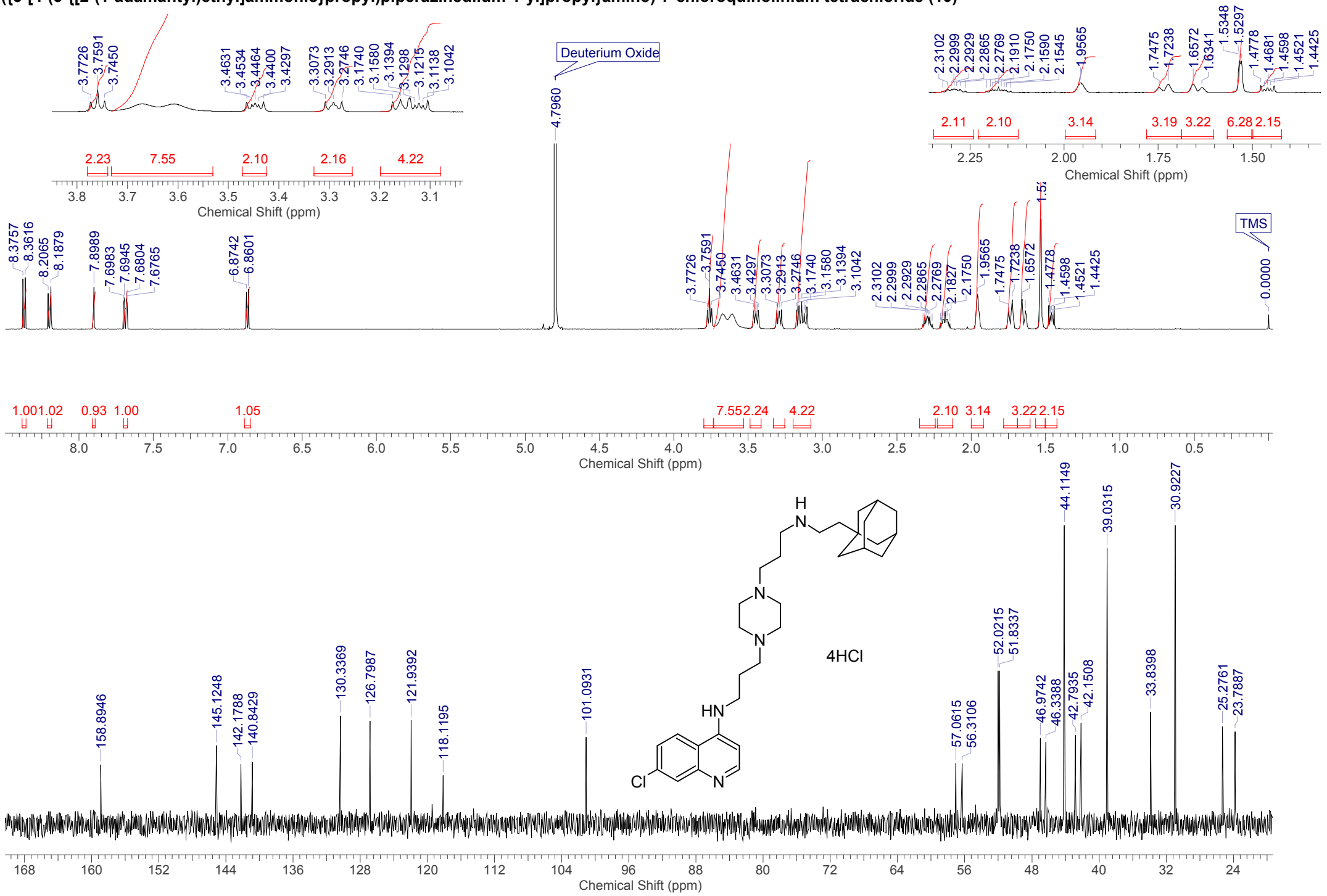

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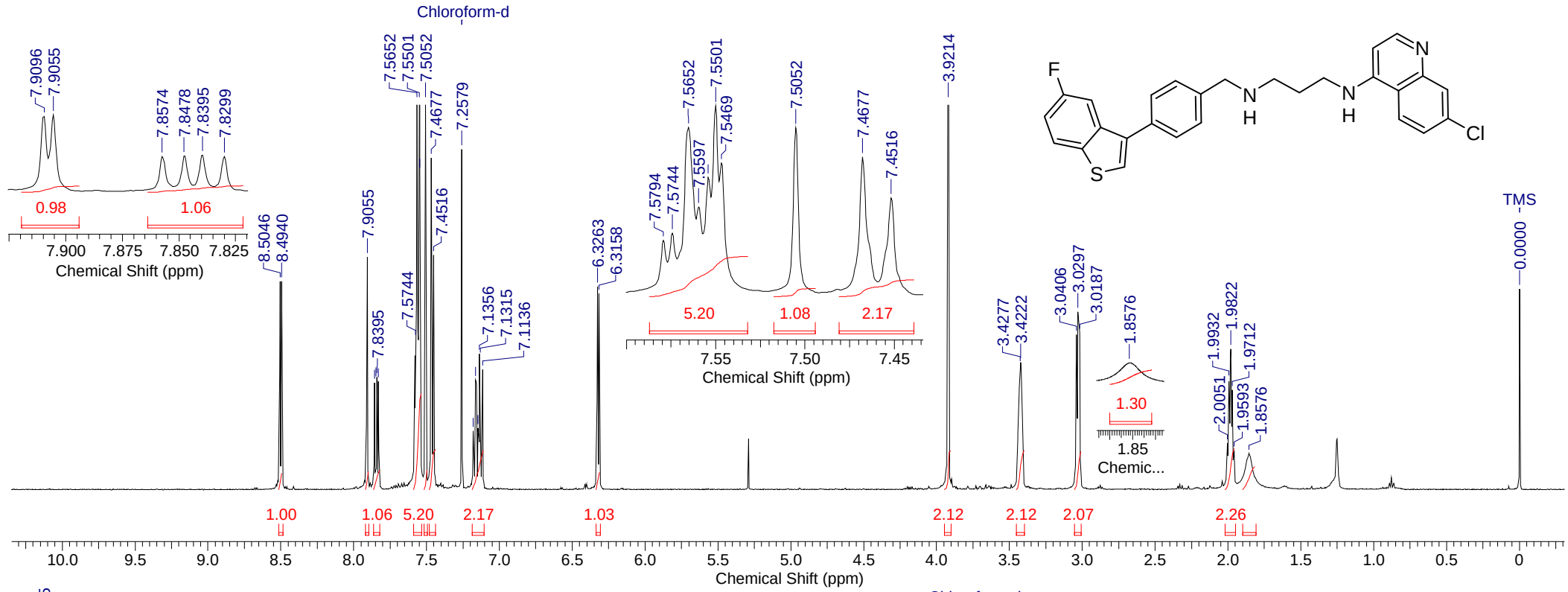

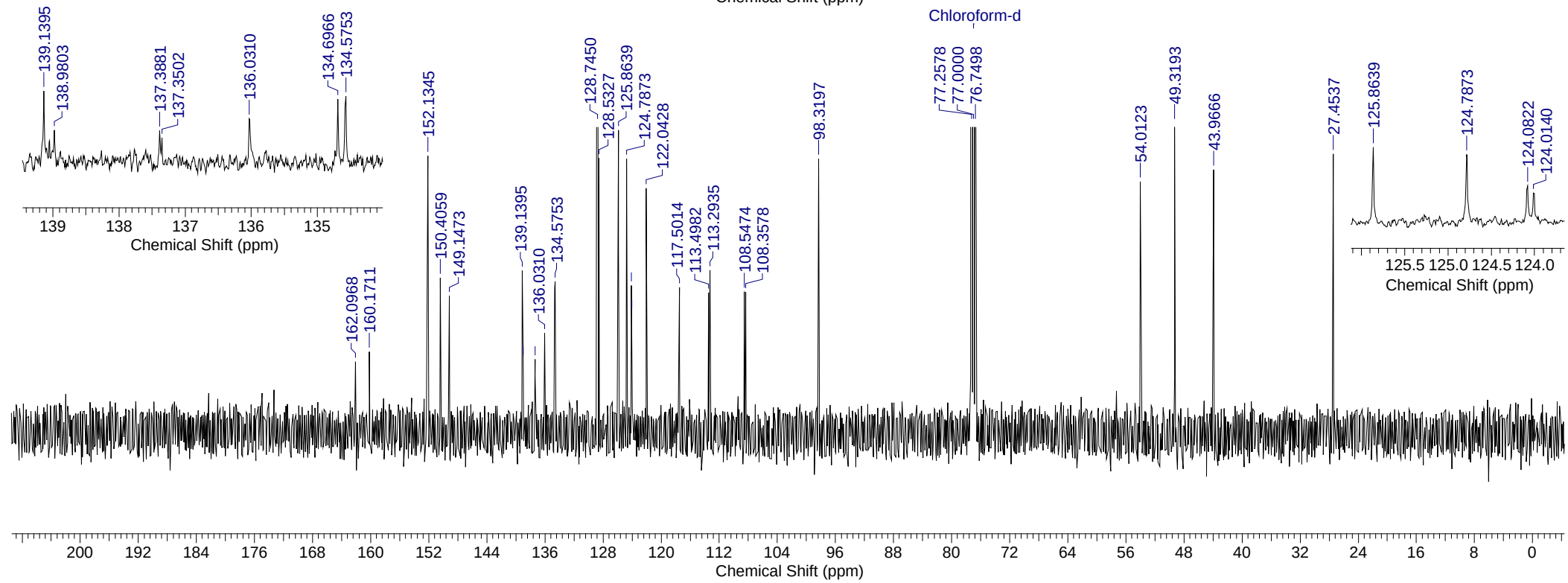

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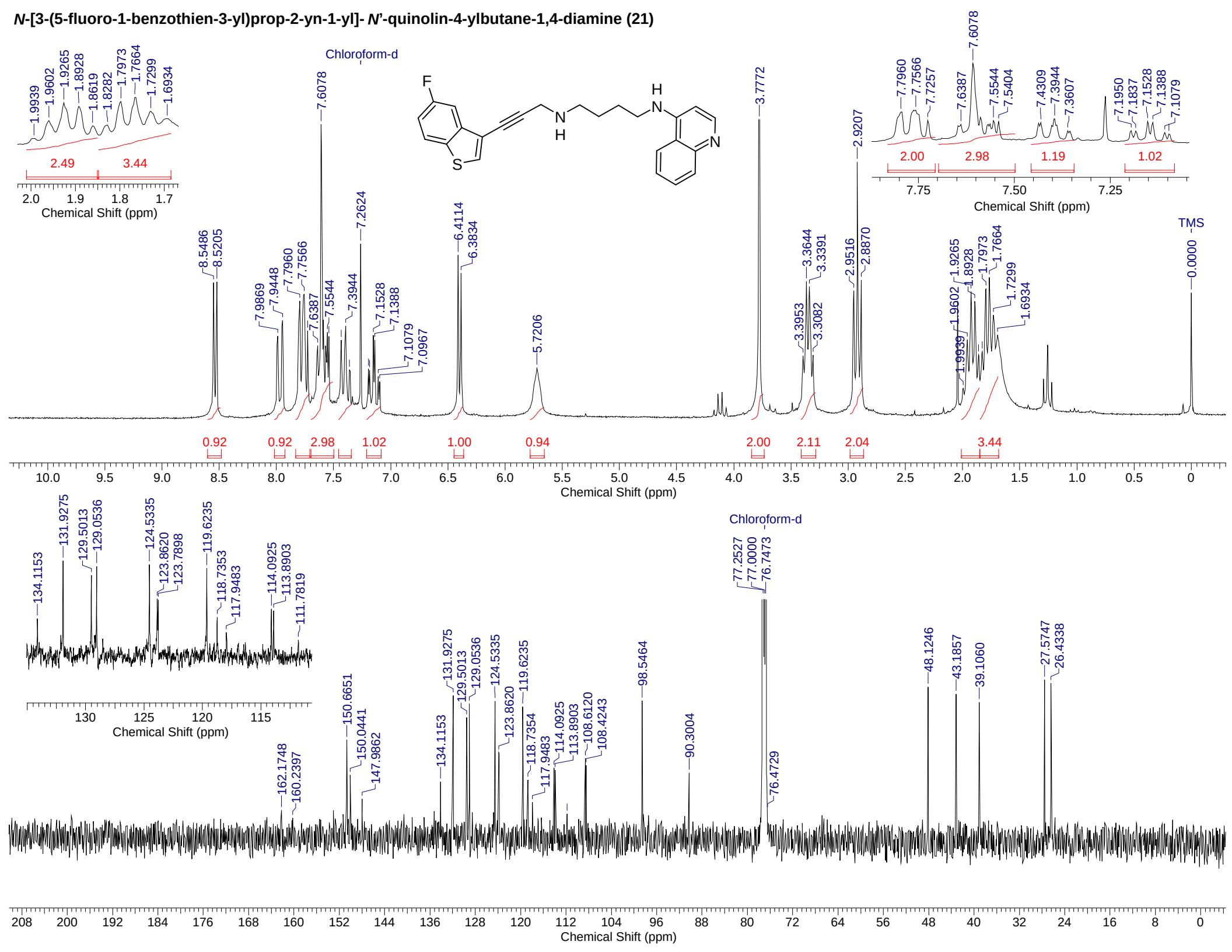
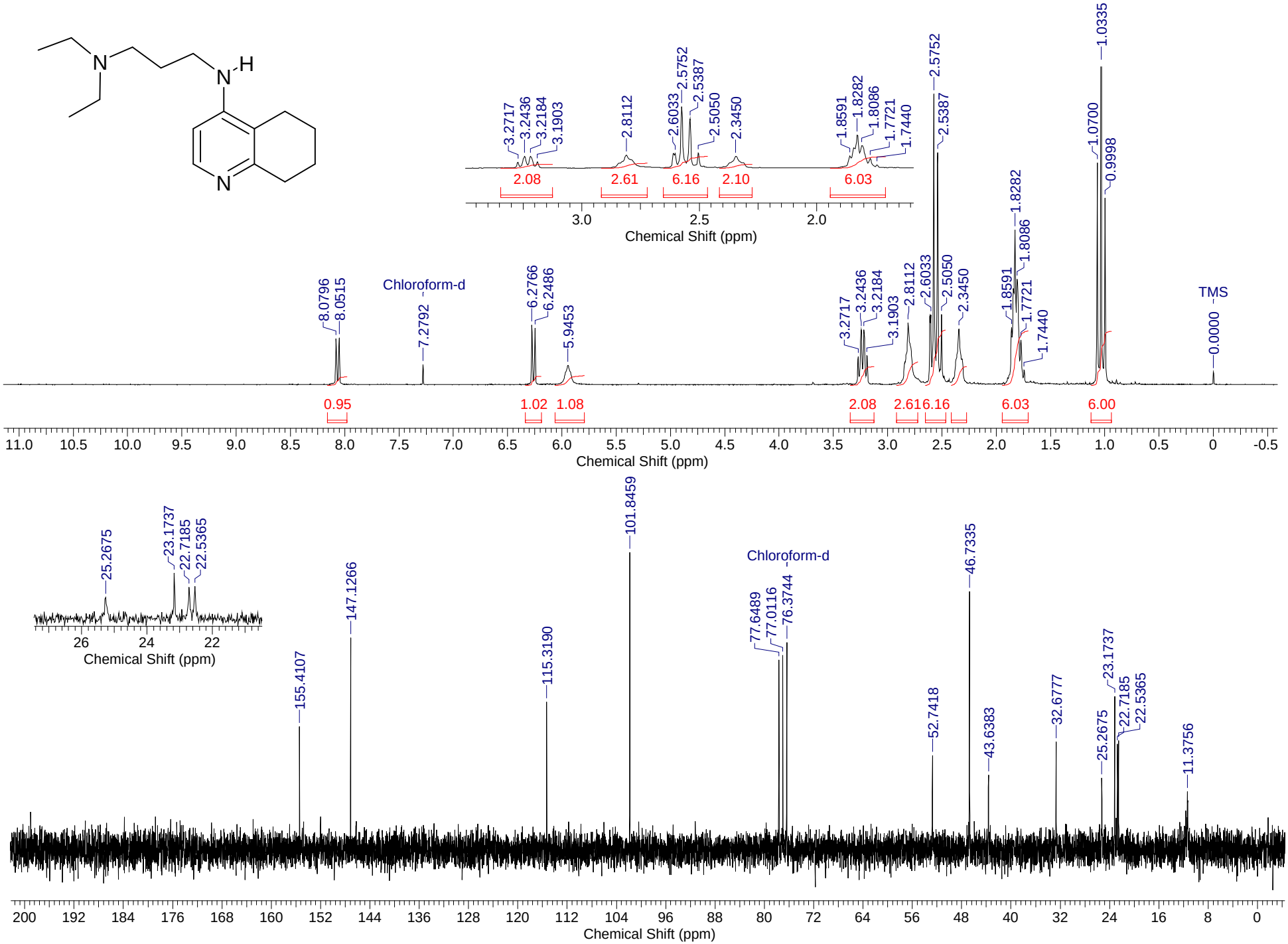


_N_,_N_-diethyl-_N'_-(5,6,7,8-tetrahydroquinolin-4-yl)propane-1,3-diamine (22)



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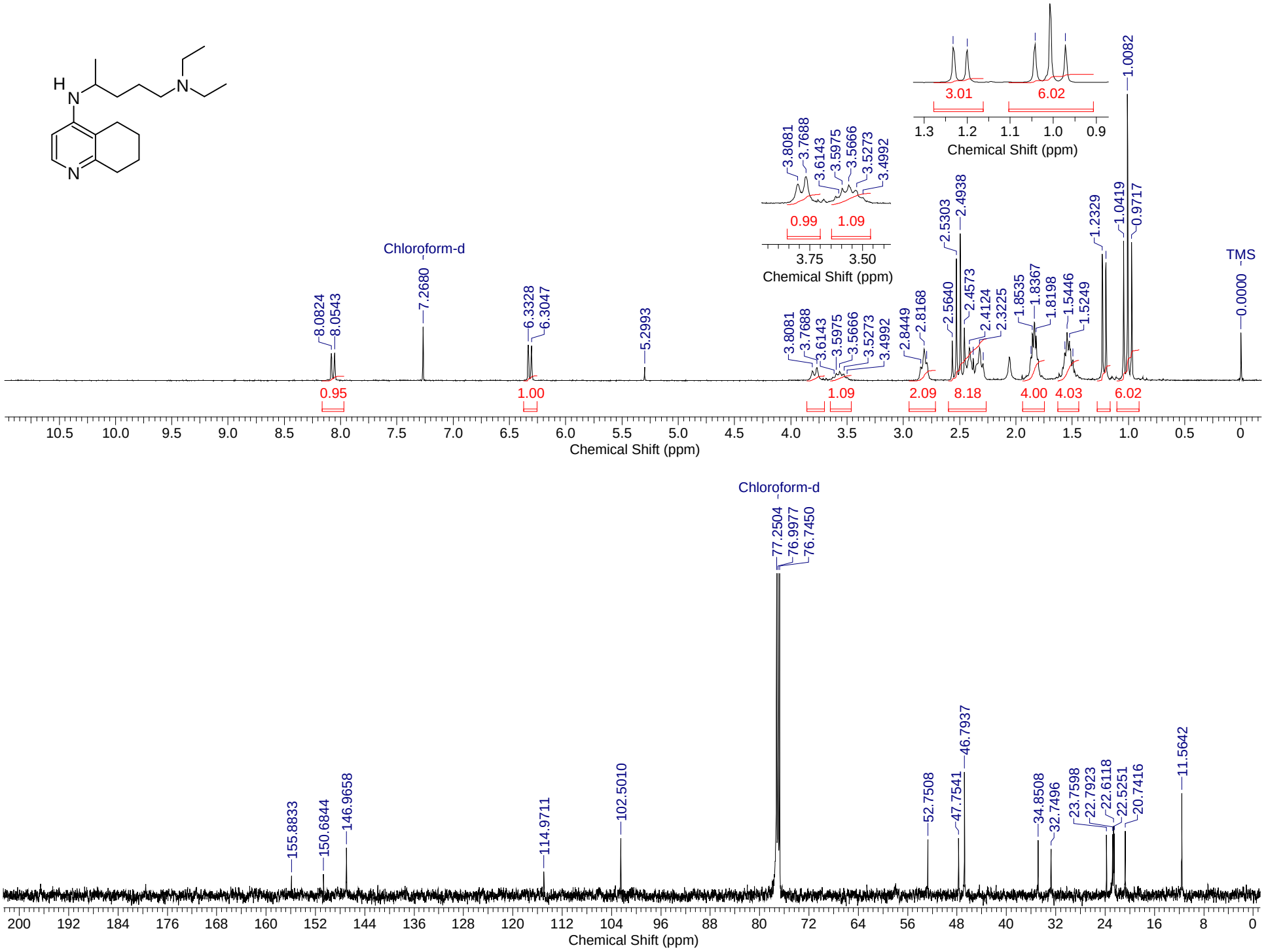
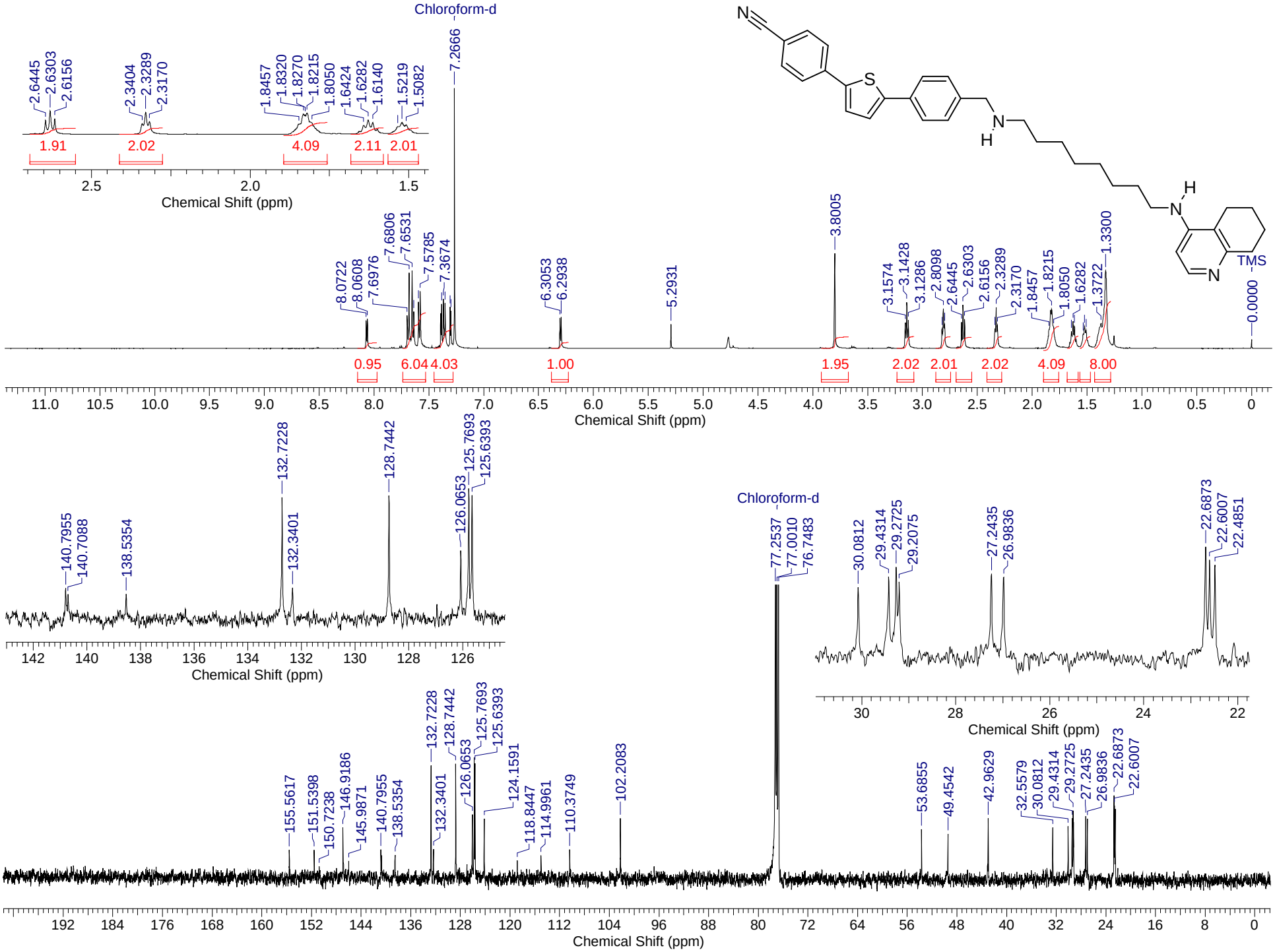


4-{5-[4-({[8-(5,6,7,8-tetrahydroquinolin-4-ylamino)octyl]amino}methyl)phenyl]-2-thienyl}benzonitrile (24)



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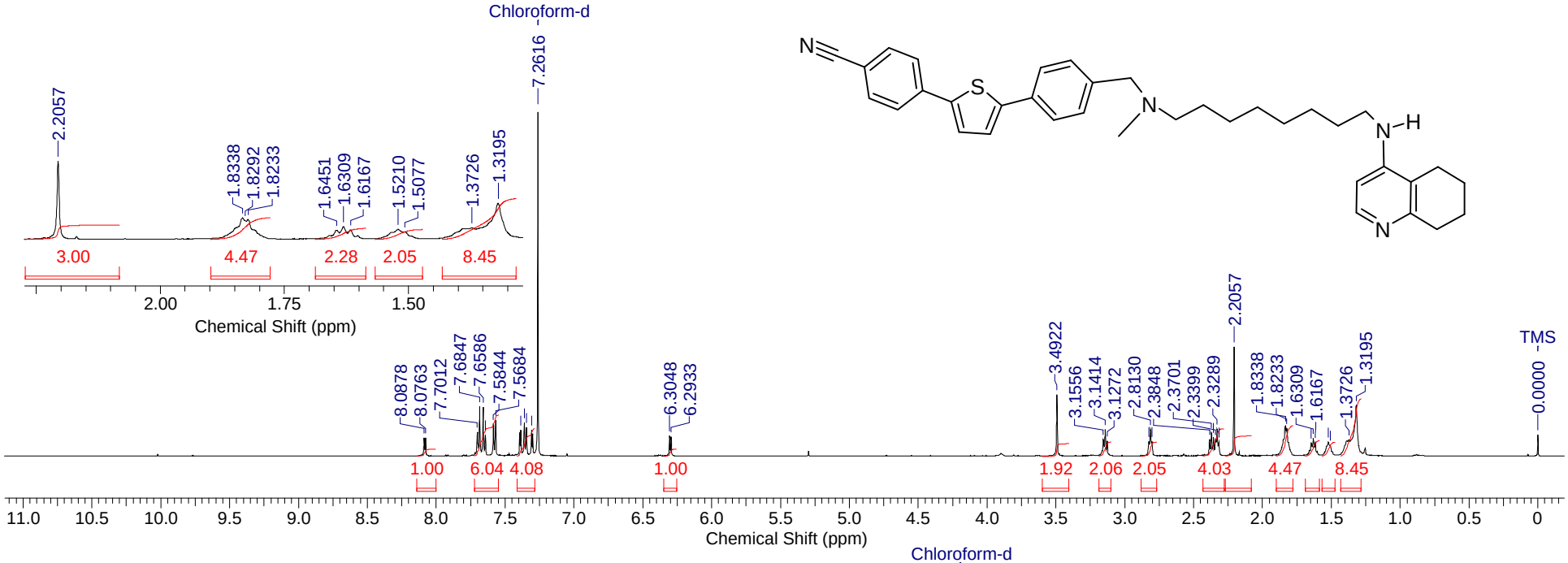
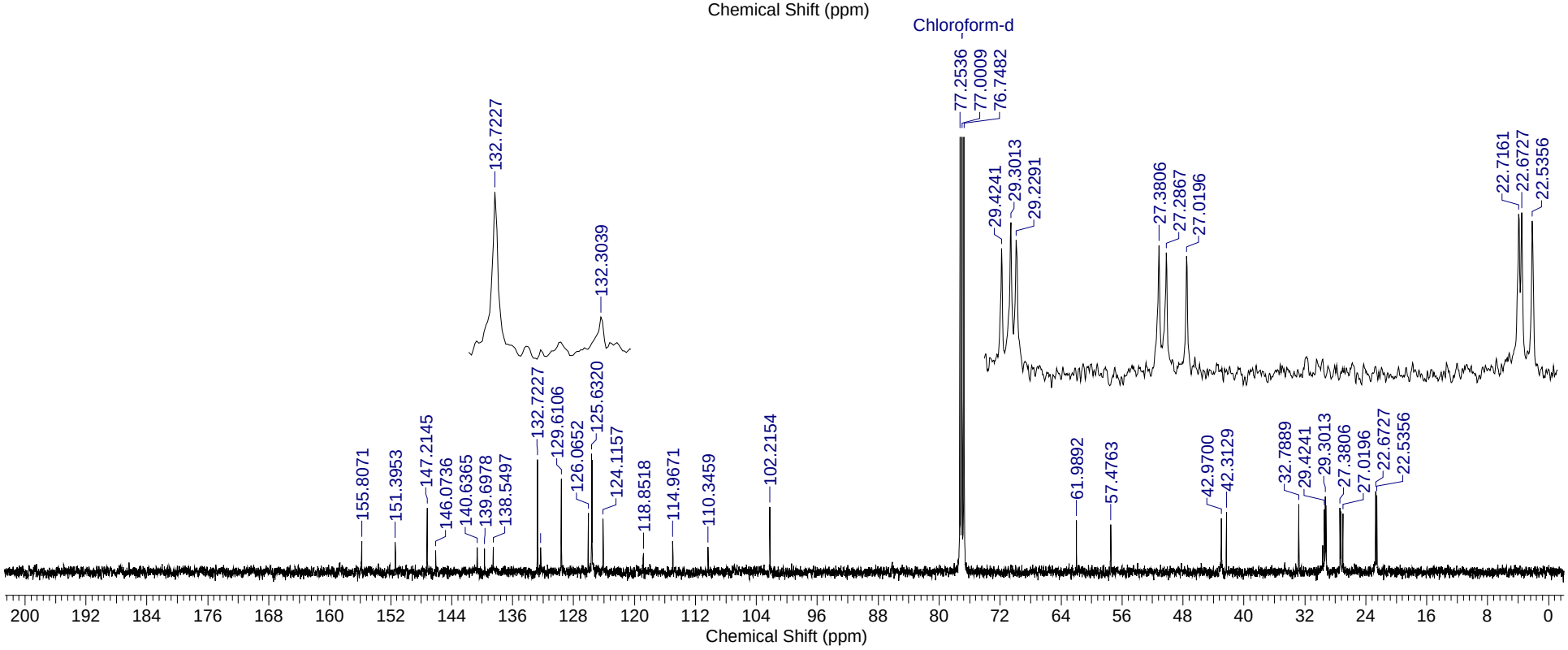
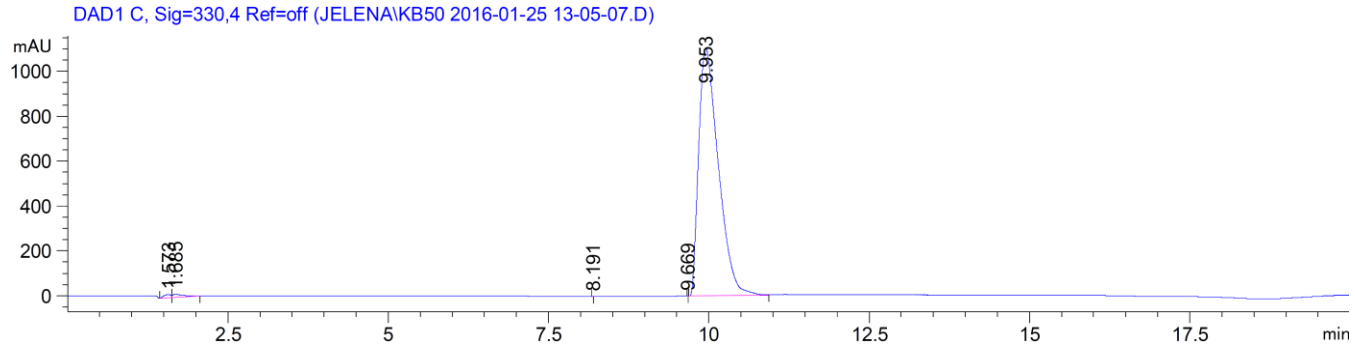




HPLC analyses for purity

Compound: 1

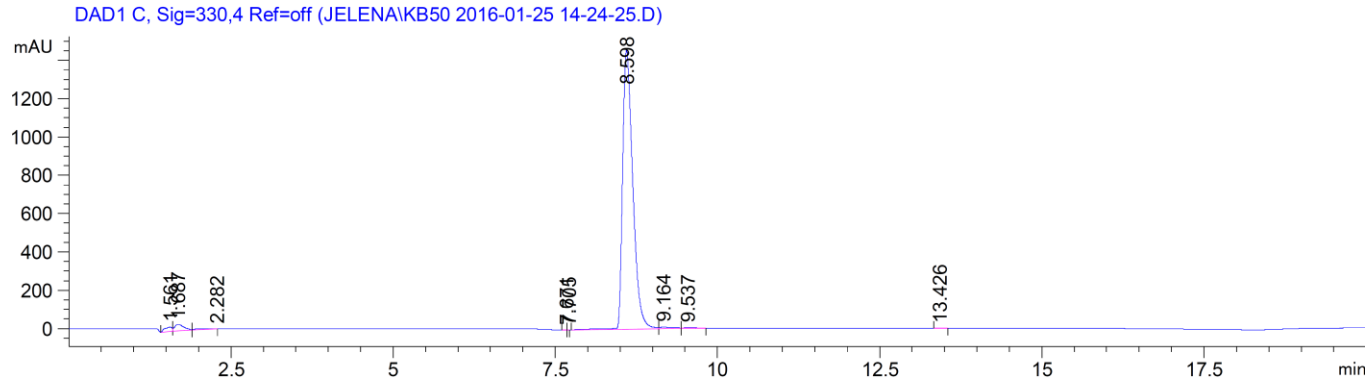
Method A



Signal 3: DAD1 C, Sig=330,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.573	BV	0.1036	105.40859	13.96111	0.4439
2	1.685	VB	0.1366	152.66585	14.41371	0.6430
3	8.191	BB	0.0147	5.69913e-2	5.70250e-2	2.400e-4
4	9.669	BB	0.0107	4.45698e-2	6.36685e-2	1.877e-4
5	9.953	BV	0.2998	2.34859e4	1103.46313	98.9127
Totals :				2.37441e4	1131.95866	

Method B

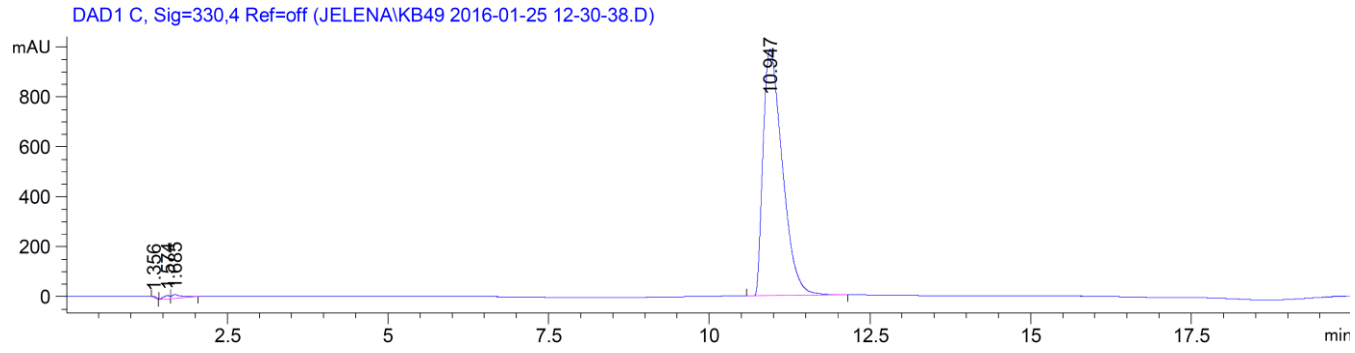


Signal 2: DAD1 C, Sig=330,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.561	BV	0.1057	184.85255	23.14280	1.1092
2	1.687	VV	0.1447	348.73328	34.72594	2.0926
3	2.282	VB	3.8846	76.79463	2.30754e-1	0.4608
4	7.671	BV	0.0482	7.93518e-1	2.00216e-1	4.762e-3
5	7.705	VB	0.0262	2.14119e-1	1.05508e-1	1.285e-3
6	8.598	BV	0.1665	1.59055e4	1454.88940	95.4426
7	9.164	VV	0.1729	111.48343	7.58695	0.6690
8	9.537	VB	0.1611	33.36453	2.46150	0.2002
9	13.426	VB	0.0739	3.25362	5.24656e-1	0.0195
Totals :				1.66650e4	1523.86772	

Compound: 2

Method A



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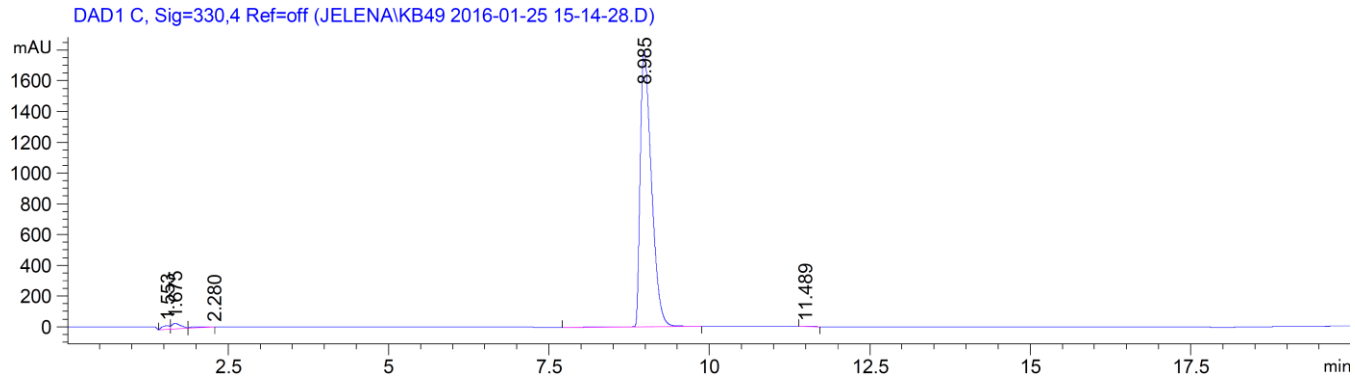
2	1.574	BV	0.0928	88.62122	12.80265	0.4264
3	1.685	VB	0.1320	154.20041	15.25146	0.7419
4	10.947	VB	0.2979	2.05254e4	987.72833	98.7487
Totals :				2.07855e4	1019.07135	

Method B



Signal 2: DAD1 C, Sig=330,4 Ref=off

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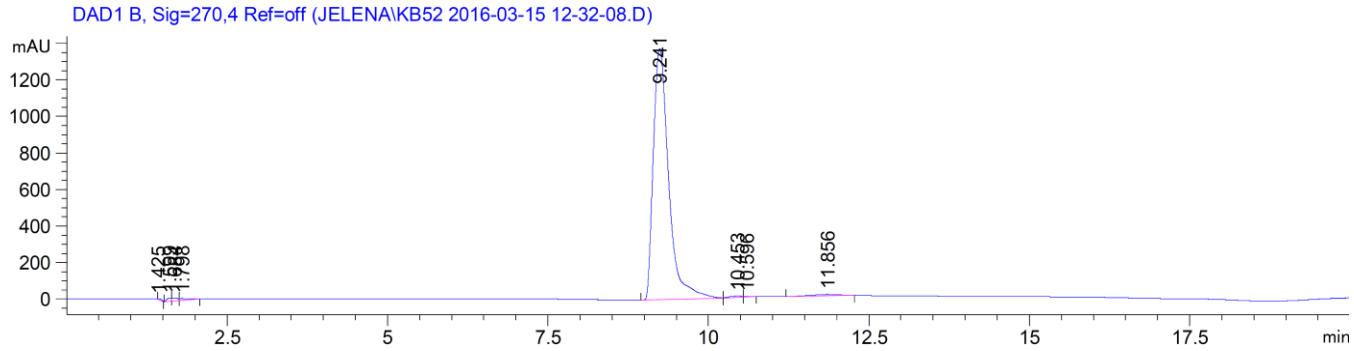
1	1.553	BV	0.1005	178.95872	23.71483	0.7923
2	1.675	VV	0.1382	339.58795	35.47026	1.5035
3	2.280	VB	3.6902	89.92261	2.84483e-1	0.3981
4	8.985	BV	0.1792	2.19726e4	1796.24792	97.2827
5	11.489	VB	0.1091	5.25767	5.75538e-1	0.0233
Totals :				2.25863e4	1856.29304	

Compound: 3

Method A



Signal 2: DAD1 B, Sig=270,4 Ref=off

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1	1.425	VB	0.0797	28.13734	4.19775	0.1199
2	1.599	BV	0.0751	80.66073	16.92988	0.3437
3	1.684	VV	0.0831	98.39760	15.49618	0.4193
4	1.798	VB	0.1281	109.27438	10.40016	0.4656
5	9.241	BB	0.2547	2.28007e4	1373.25891	97.1549
6	10.453	BV	0.1554	95.82644	7.43150	0.4083
7	10.596	VB	0.0894	25.37045	3.48489	0.1081
8	11.856	BB	0.3464	230.03264	7.79287	0.9802
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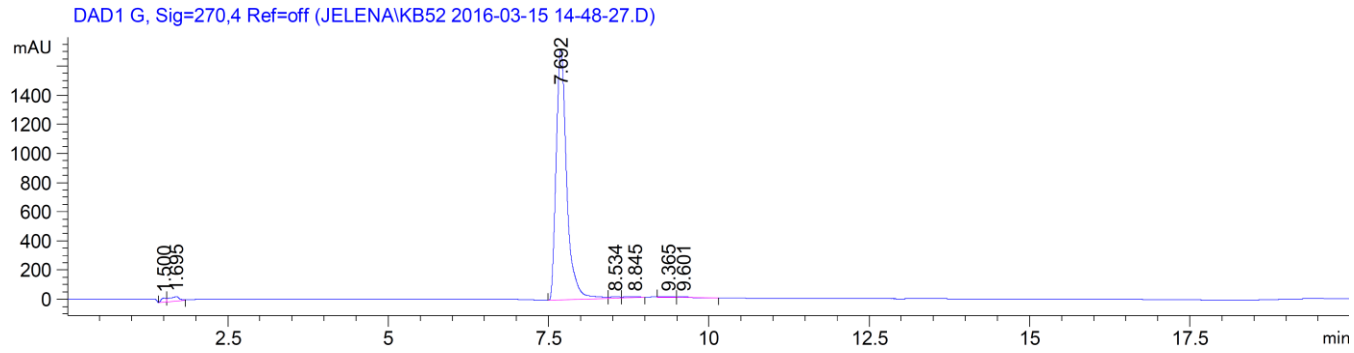
Method B



Signal 3: DAD1 G, Sig=270,4 Ref=off

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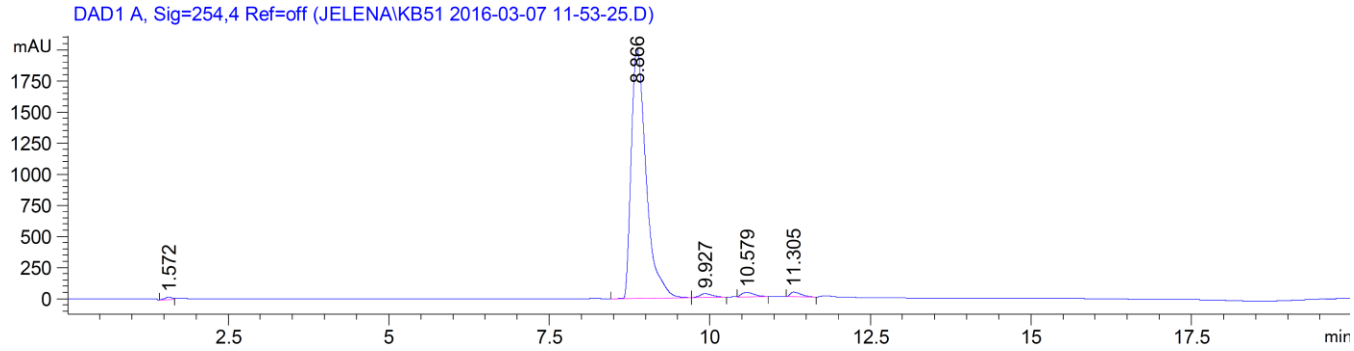
3	7.692	BV	0.1750	1.97402e4	1718.59253	95.7563
4	8.534	VV	0.1318	111.12260	9.99130	0.5390
5	8.845	VB	0.2075	105.68089	5.99840	0.5126
6	9.365	VV	0.1728	80.66315	5.50875	0.3913
7	9.601	VB	0.1474	93.21310	7.55732	0.4522
Totals :				2.06151e4	1805.16232	

Compound: 4

Method A



Signal 1: DAD1 A, Sig=254,4 Ref=off

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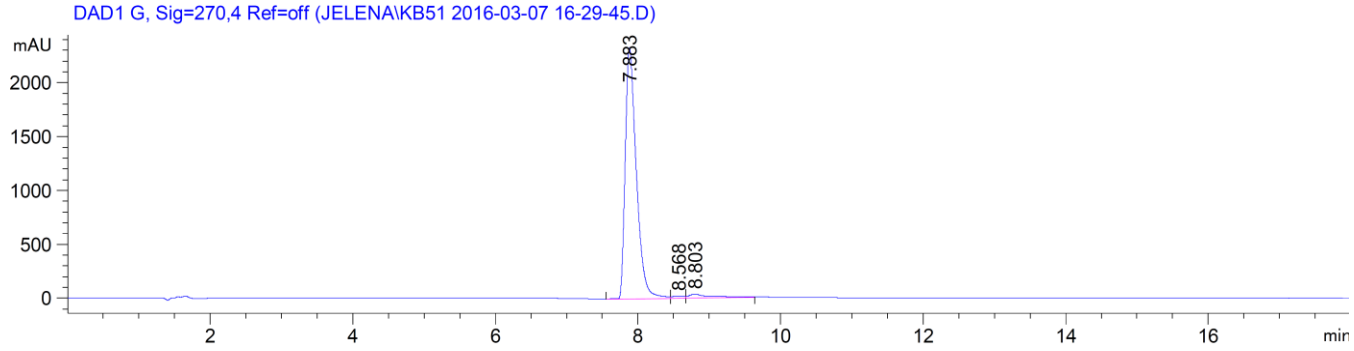
2	8.866	BV	0.2139	3.22791e4	2010.08569	95.5675
3	9.927	VB	0.1748	431.68842	30.36716	1.2781
4	10.579	VB	0.1694	464.05820	35.06033	1.3739
5	11.305	BB	0.1598	428.19977	37.19765	1.2678
Totals :				3.37762e4	2134.89236	

Method B

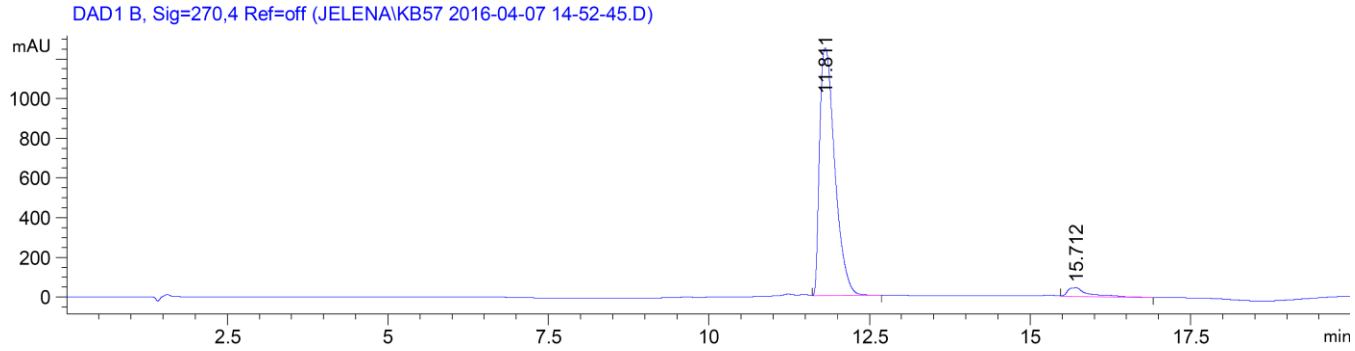


Signal 3: DAD1 G, Sig=270,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.883	BV	0.1291	2.51235e4	2333.72437	95.5612
2	8.568	VV	0.1407	242.59225	20.32733	0.9227
3	8.803	VV	0.3236	924.39185	35.64532	3.5161
Totals :				2.62905e4	2389.69701	

Compound: 5

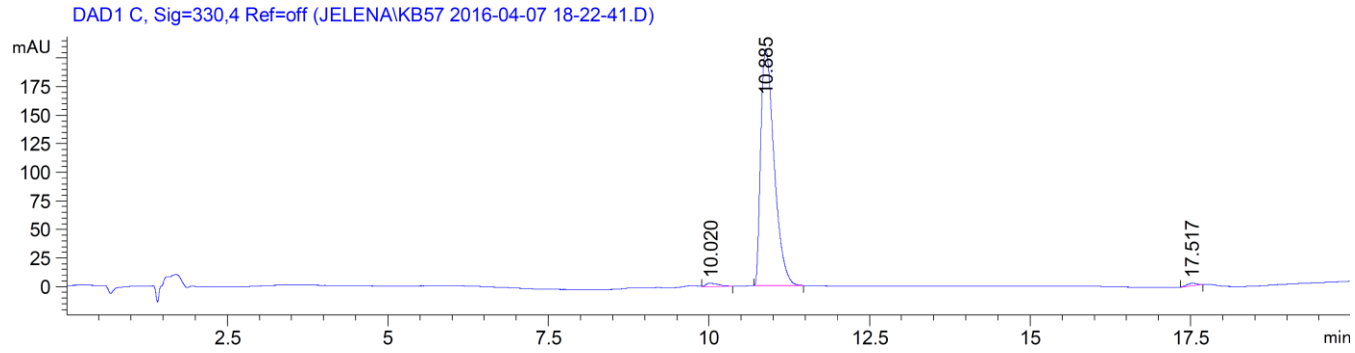
Method A



Signal 2: DAD1 B, Sig=270,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.811	VB	0.2465	2.05500e4	1248.69263	95.5095
2	15.712	VB	0.2762	966.18292	43.83290	4.4905
Totals :				2.15162e4	1292.52553	

Method B

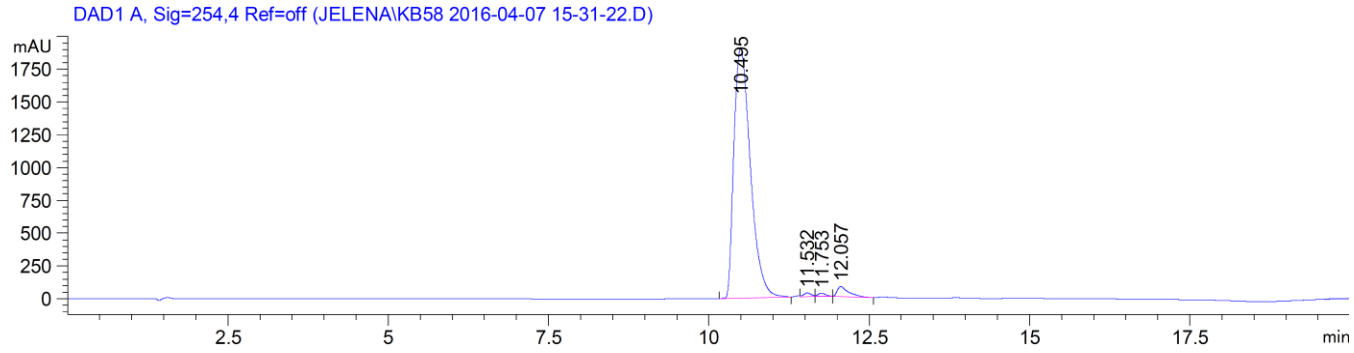


Signal 2: DAD1 C, Sig=330,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.020	VB	0.1620	42.47963	3.15679	1.3850
2	10.885	BB	0.2165	3001.71289	207.20801	97.8644
3	17.517	BB	0.1214	23.02526	2.24897	0.7507
Totals :				3067.21778	212.61377	

Compound: 6

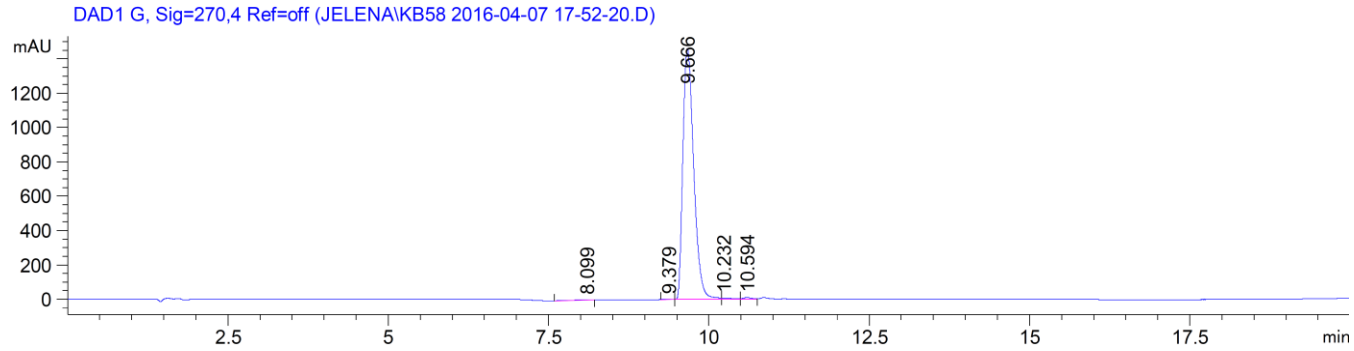
Method A



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.495	BB	0.2137	3.40220e4	1902.29553	96.0275
2	11.532	VV	0.1148	240.47559	27.96380	0.6787
3	11.753	VB	0.1193	207.88483	25.17498	0.5868
4	12.057	BB	0.1772	959.07672	76.53194	2.7070
Totals :				3.54294e4	2031.96626	

Method B

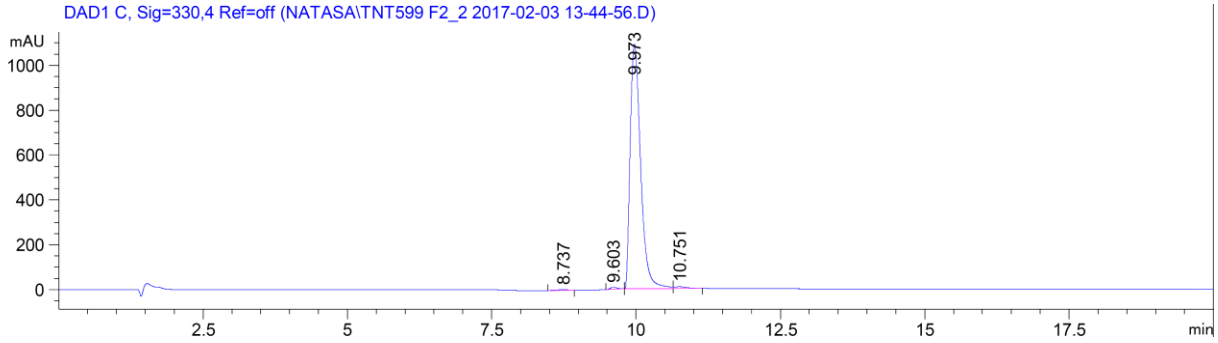


Signal 3: DAD1 G, Sig=270,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.099	BV	0.3515	40.44973	1.35017	0.2329
2	9.379	VB	0.0824	8.81246	1.29542	0.0507
3	9.666	BV	0.1809	1.71276e4	1459.74524	98.6289
4	10.232	VV	0.1388	94.94499	8.09829	0.5467
5	10.594	VV	0.1184	93.89258	9.45137	0.5407
Totals :				1.73657e4	1479.94048	

Compound: 10

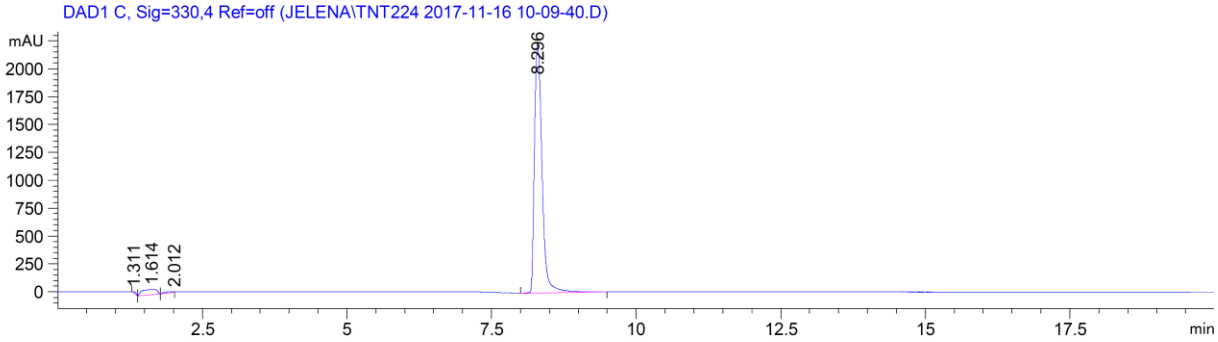
Method A



Signal 2: DAD1 C, Sig=330,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.737	BV	0.1365	40.78170	3.53764	0.2911
2	9.603	BB	0.1154	84.12697	9.09872	0.6006
3	9.973	BV	0.1964	1.37720e4	1089.88208	98.3134
4	10.751	VV	0.1651	111.35114	7.96709	0.7949
Totals :				1.40083e4	1110.48554	

Method B

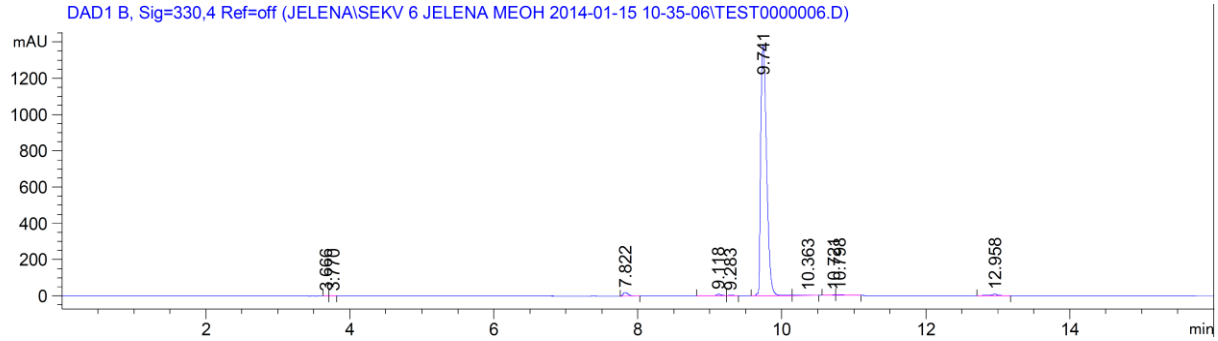


Signal 2: DAD1 C, Sig=330,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.311	BB	0.0792	49.82119	9.34718	0.2319
2	1.614	BB	0.2088	841.34064	47.57282	3.9170
3	2.012	BV	0.2952	114.31578	4.57146	0.5322
4	8.296	BB	0.1421	2.04739e4	2230.87305	95.3189
Totals :				2.14793e4	2292.36451	

Compound: 15

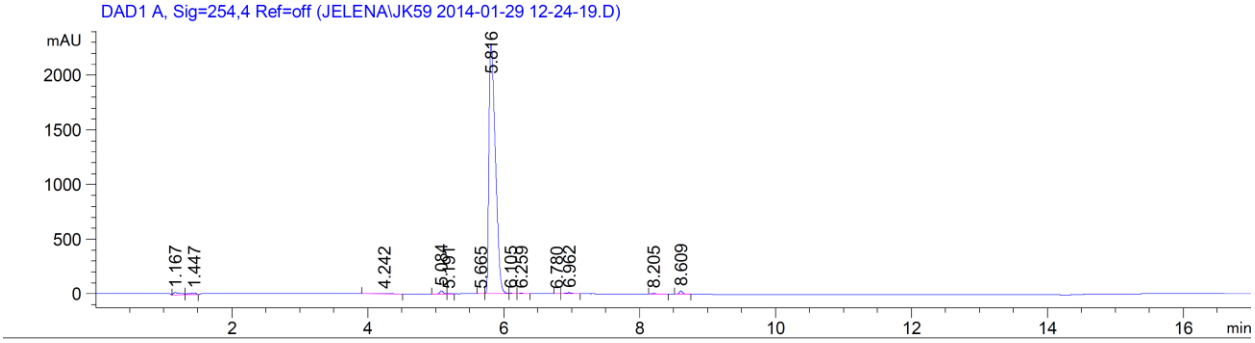
Method C



Signal 2: DAD1 B, Sig=330,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.666	VV	0.0499	5.86679	1.61452	0.0725
2	3.770	VV	0.0615	6.42468	1.46846	0.0794
3	7.822	BB	0.0736	91.23423	19.33337	1.1270
4	9.118	BV	0.0771	43.22337	8.24990	0.5339
5	9.283	VV	0.0691	12.93283	2.44820	0.1598
6	9.741	BV	0.0899	7817.75244	1383.93896	96.5682
7	10.363	VB	0.0935	14.27669	1.80958	0.1764
8	10.721	BV	0.0606	14.11273	3.25163	0.1743
9	10.798	VB	0.0923	39.79552	5.57518	0.4916
10	12.958	BB	0.0878	49.95594	7.73735	0.6171
Totals :				8095.57523	1435.42716	

Method D

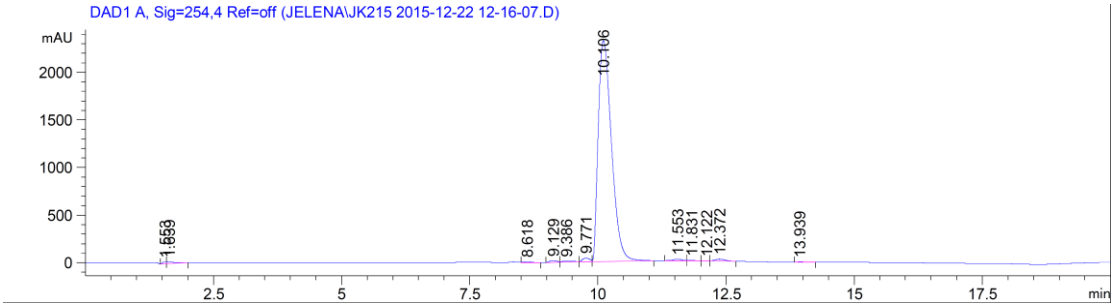


Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.167	BV	0.1030	153.61269	20.72488	0.9738
2	1.447	VB	0.1062	122.89980	13.82392	0.7791
3	4.242	BB	0.1556	56.76239	4.64547	0.3598
4	5.084	BV	0.0498	90.18621	27.49329	0.5717
5	5.191	VV	0.0515	6.70909	1.58050	0.0425
6	5.665	BV	0.0465	5.10729	1.61156	0.0324
7	5.816	VV	0.1028	1.50860e4	2290.39307	95.6341
8	6.105	VV	0.0573	18.89536	4.61160	0.1198
9	6.259	VB	0.0505	23.72610	7.00373	0.1504
10	6.780	VV	0.0526	8.14344	2.31199	0.0516
11	6.962	VB	0.1128	72.58609	9.32257	0.4601
12	8.205	VB	0.0589	26.87801	6.97987	0.1704
13	8.609	VB	0.0545	103.20499	29.03672	0.6542
Totals :				1.57747e4	2419.53917	

Compound: 21

Method A

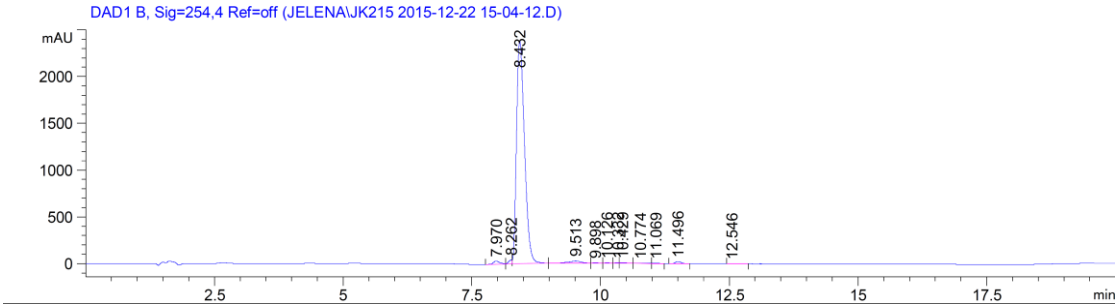


Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.553	BV	0.0776	91.92958	18.79401	0.2130
2	1.639	VB	0.1344	198.15492	19.69478	0.4591
3	8.618	VB	0.1283	111.68575	11.30480	0.2587
4	9.129	BV	0.1354	174.10493	16.66947	0.4033
5	9.386	VB	0.1657	145.31332	10.35561	0.3366
6	9.771	BV	0.1552	355.89175	36.51839	0.8245
7	10.106	VB	0.2107	4.14863e4	2319.59961	96.1112
8	11.553	VV	0.1670	213.49384	16.01798	0.4946
9	11.831	VB	0.1244	47.32322	4.58520	0.1096
10	12.122	BV	0.0835	16.24580	2.32430	0.0376
11	12.372	VB	0.1667	292.75635	21.06087	0.6782
12	13.939	BB	0.1293	31.70451	3.01281	0.0734

Totals : 4.31649e4 2479.93781

Method B



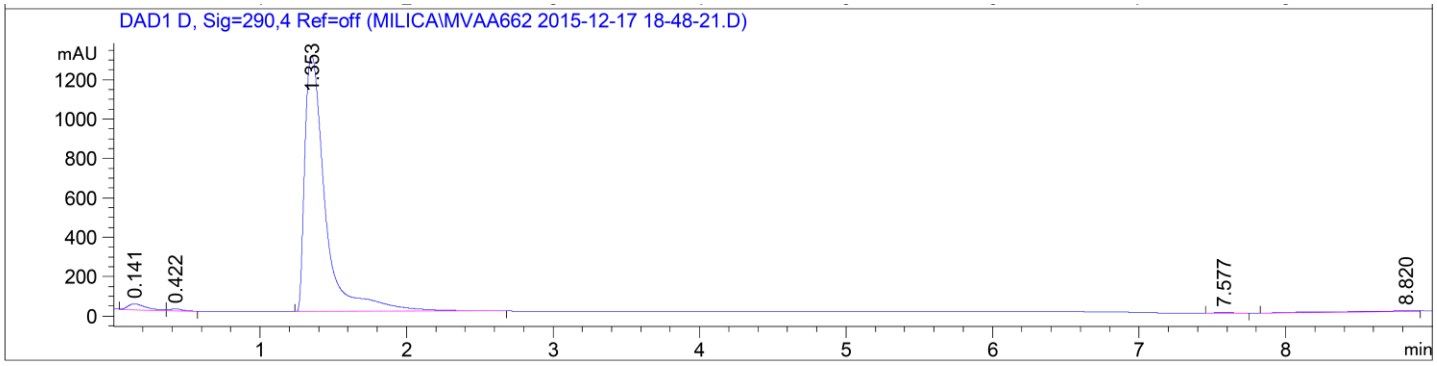
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.970	BV	0.1311	279.44455	32.74783	1.0427
2	8.262	VV	0.0693	176.40025	40.87649	0.6582
3	8.432	VB	0.1655	2.56459e4	2383.74829	95.6892
4	9.513	BV	0.2027	347.04858	21.80587	1.2949
5	9.898	VB	0.0984	16.29854	2.05749	0.0608
6	10.126	BV	0.0821	16.34438	2.36577	0.0610
7	10.332	VV	0.0655	22.35339	4.87294	0.0834
8	10.429	VV	0.1072	61.95589	7.24741	0.2312
9	10.774	VV	0.1491	39.22920	3.11046	0.1464
10	11.069	VB	0.0946	14.12029	1.81806	0.0527
11	11.496	BB	0.1218	160.73245	21.35513	0.5997
12	12.546	BB	0.1077	21.43447	2.42209	0.0800

Totals : 2.68013e4 2524.42784

Compound: 22

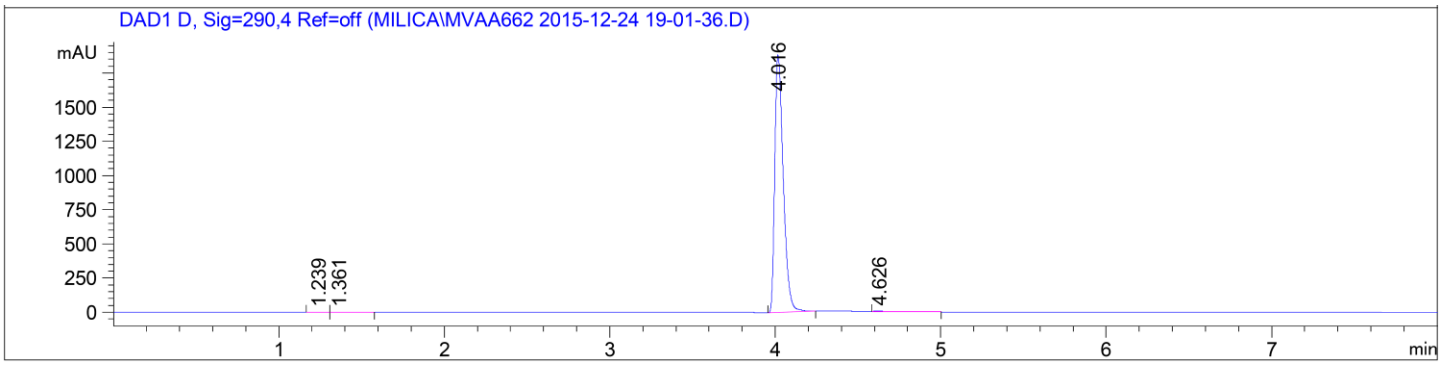
Method A



Signal 4: DAD1 D, Sig=290,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.141	VV	0.1171	247.75066	29.47381	1.8894
2	0.422	VB	0.0820	55.16560	9.61117	0.4207
3	1.353	BB	0.1484	1.26743e4	1298.76404	96.6572
4	7.577	BB	0.1037	21.18176	2.44210	0.1615
5	8.820	BV	0.6545	114.23597	2.04417	0.8712
Totals :				1.31126e4	1342.33529	

Method E

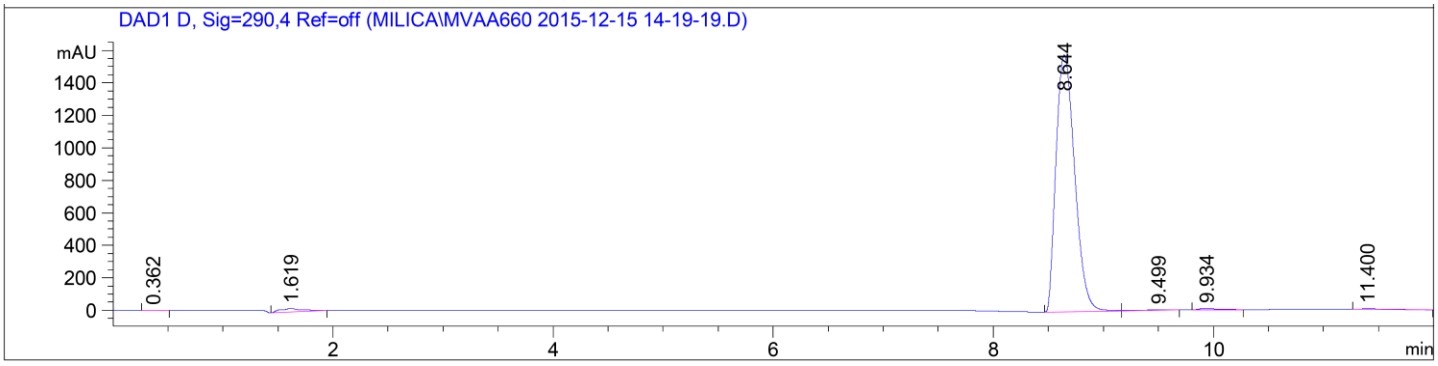


Signal 4: DAD1 D, Sig=290,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.239	VV	0.0671	10.42186	1.86773	0.1533
2	1.361	VB	0.0689	17.28675	3.08195	0.2542
3	4.016	BV	0.0543	6759.96680	1885.48987	99.4120
4	4.626	VB	0.0886	12.27417	1.66243	0.1805
Totals :				6799.94957	1892.10197	

Compound: 23

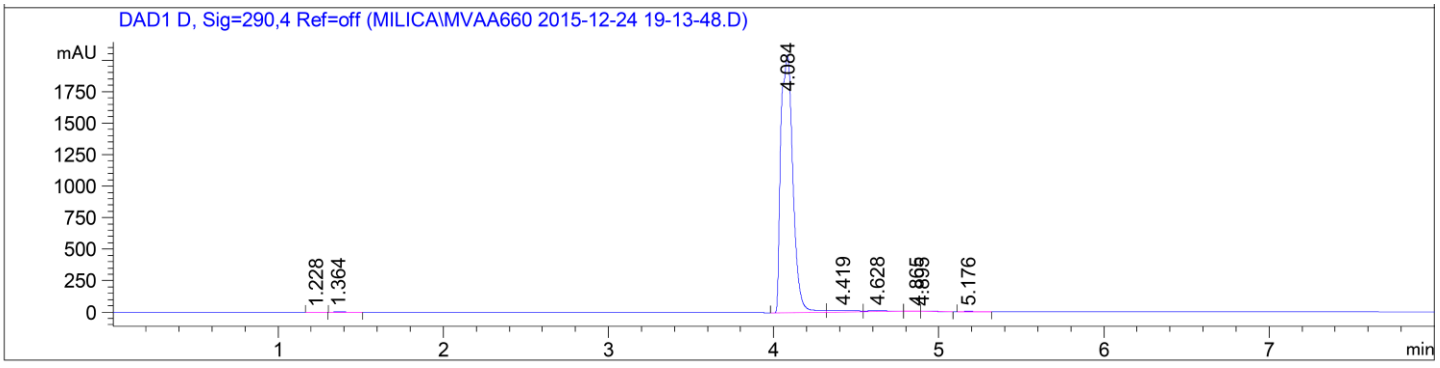
Method A



Signal 4: DAD1 D, Sig=290,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.362	BB	0.0787	7.39480	1.11772	0.0387
2	1.619	BB	0.1825	307.33722	21.53188	1.6077
3	8.644	BV	0.1402	1.85912e4	1581.15515	97.2543
4	9.499	VV	0.1675	55.64240	3.95747	0.2911
5	9.934	BB	0.1335	90.59611	8.09747	0.4739
6	11.400	BBA	0.1606	63.90107	4.73127	0.3343
Totals :				1.91160e4	1620.59096	

Method E

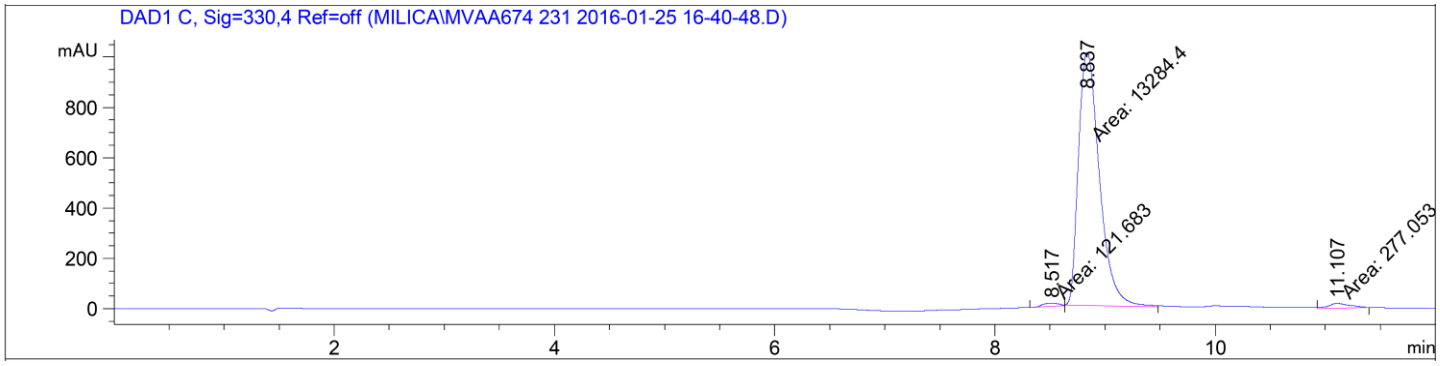


Signal 4: DAD1 D, Sig=290,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.228	VB	0.0712	10.64459	1.96605	0.0999
2	1.364	BV	0.0846	17.77066	2.89378	0.1667
3	4.084	BV	0.0690	1.03580e4	2046.91760	97.1763
4	4.419	VV	0.1378	161.83618	14.11464	1.5183
5	4.628	VB	0.1022	84.30206	10.55695	0.7909
6	4.865	BV	0.0477	5.33605	1.34785	0.0501
7	4.895	VB	0.0677	8.40072	1.49150	0.0788
8	5.176	BB	0.0640	12.68676	2.42771	0.1190
Totals :				1.06590e4	2081.71608	

Compound: 24

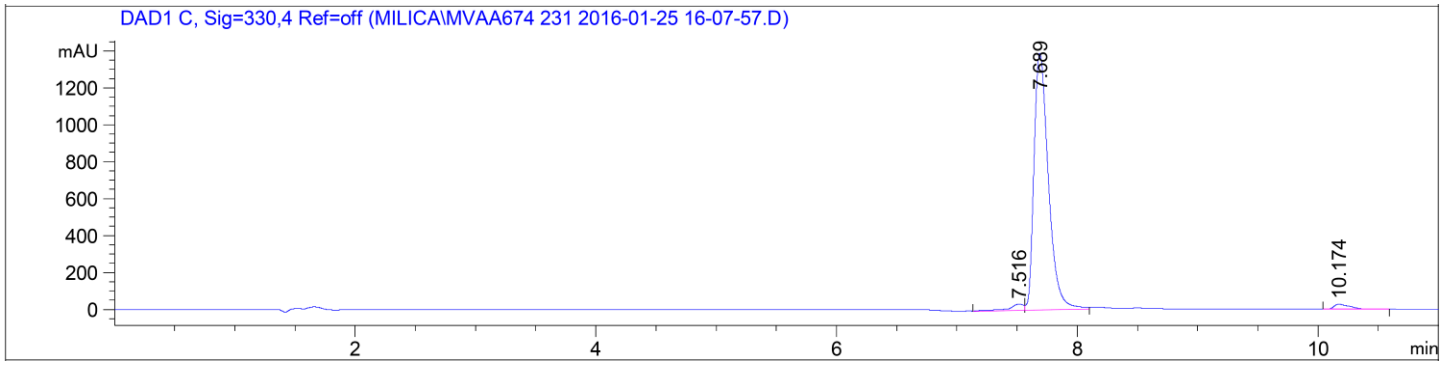
Method A



Signal 3: DAD1 C, Sig=330,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.517	MM	0.1654	121.68285	12.26426	0.8893
2	8.837	MM	0.2204	1.32844e4	1004.56268	97.0859
3	11.107	MM	0.1651	277.05350	19.78963	2.0248
Totals :				1.36831e4	1036.61658	

Method B

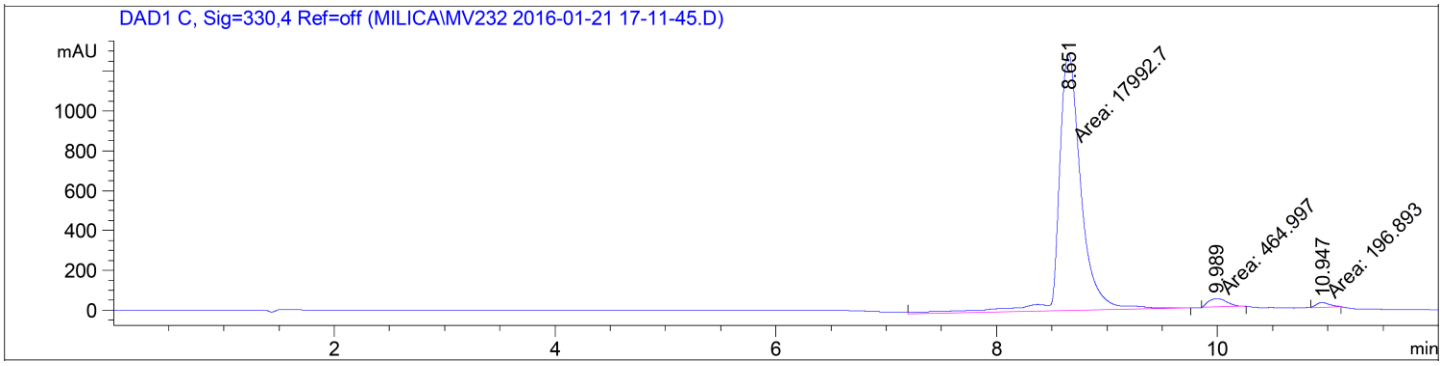


Signal 3: DAD1 C, Sig=330,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.516	BV	0.1245	288.66171	34.02340	2.3821
2	7.689	VV	0.1286	1.15766e4	1390.29077	95.5321
3	10.174	BB	0.1275	252.75702	27.42595	2.0858
Totals :				1.21180e4	1451.74013	

Compound: 25

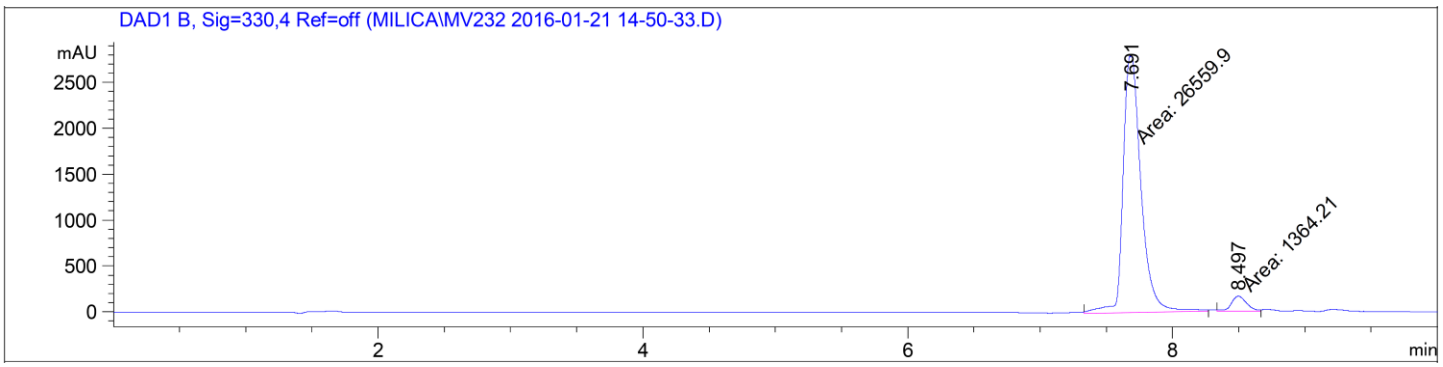
Method A



Signal 3: DAD1 C, Sig=330,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.651	MM	0.2323	1.79927e4	1290.94250	96.4519
2	9.989	MM	0.1925	464.99719	40.25417	2.4927
3	10.947	MM	0.1337	196.89345	24.54042	1.0555
Totals :				1.86546e4	1355.73710	

Method B



Signal 2: DAD1 B, Sig=330,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.691	MM	0.1576	2.65599e4	2808.66309	95.1146
2	8.497	MM	0.1368	1364.21326	166.19298	4.8854
Totals :				2.79241e4	2974.85606	